
4th and 5th Year Medicine

Study Notes

Edited by David Tripp

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Volume 1

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*To Helen, Laura and Esther
My precious wife and daughters
Thanks for your support and patience*

Credits and Introduction

This workbook collates all the study material lavished upon us in the 4th and 5th Year Medicine course taught at the Wellington School of Medicine. It is an attempt to organise and summarise the zillion and one things that of course you should know.

This second edition also includes further material gained as a Trainee Intern. Thankfully this added to the practical material without impacting on the bulk! Revising these notes also gave me a chance to remove another round of bloopers.

*This document is intended to help you cram for exams. **It is not intended as a clinical reference, and should not be used for making real life decisions. Find something (much) more reliable. I have endeavoured to be as accurate as possible, but a patient on the end of a needle deserves better than the ravings of a 6th year student.***

Sections whose headers are marked with an '*' are sections I compiled from books – these were not taught as discrete topics, but I thought they should be in here.

I am indebted to Matthew Kelly for his review of parts of this document (thanks Matt!) and the many lecturers who taught us. Where I drew from substantial handouts, these are referenced.

I have also used the following books:

- Oxford Handbook of Clinical Medicine, 4th Edition, R A Hope, J M Longmore, S K McManus and C A Wood-Allum, Oxford University Press, 1998
- N J Talley and S O'Connor, Clinical Examination – a Systematic Guide to Physical Diagnosis, Third Edition, MacLennan & Petty Pty Ltd, 1998
- T J B Maling and C D Burgess, Clinical Pharmacology and Therapeutics, 9th Edition, Wellington School of Medicine, 2000

These are good books – buy them!

Feedback – especially any bloopers – would be most welcome. Email them to me at David.Tripp@xtra.co.nz.

Enjoy!

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Relationship to Wellington School of Medicine Runs

Run/Module	Where to find the material from that run in this document
Clinical Skills	Material from this run is included in the relevant systems chapters, mainly Cardiovascular, Respiratory and Renal. Endocrine is a separate chapter.
Neuro-sensory	All in the Neuro-sensory Chapter
Health Care and the Elderly	All in the Health Care of the Elderly Chapter, or referenced from there
Psychological Medicine	All in the Psychological Medicine Chapter
Gut	Mainly in the Gastro-Intestinal Chapter (incorporating the substantial run handout). IV Fluids and Nutrition are in the Surgery and Fluid Management Chapter.
Community Medicine/GP Run	Material from this run is scattered through the relevant system chapters. Dermatology is in the Skin Chapter, Consultation Skills is in the Patient Management Chapter, Grief and Terminal Illness is in Psychological Medicine Chapter, Screening and the Health System in NZ is in the Public Health Chapter, Sexual Health in the Reproductive and Obstetrics Chapter
Anaesthetics and Emergency	Material is split across the Anaesthetics Chapter and the Emergency Management Chapter, or referenced from there
Women's, Sexual and Reproductive Health	All in the Obstetrics and Gynaecology Chapter, except for Urinary Incontinence in the Renal Chapter and Post-natal depression in the Psychological Medicine Chapter
Public Health	All in the Public Health Chapter
Paediatrics	Mainly in the paediatrics Chapter. Meningitis is in the Infectious Diseases chapter and some paediatric skin conditions are in the Skin Chapter. UTIs are covered in the Renal and Genitourinary Chapter
Musculo-Skeletal	All in the Musculo-skeletal chapter or referenced from there
Medicine	In the Cardiovascular, Respiratory, Renal or Endocrine Chapter
Pathology	Pathology of specific systems is merged into those system chapters. Haematology material is the Haematology Chapter, in the Blood Tests section of Patient Management Chapter, and Blood Products section of the Surgery and Fluid Management Chapter. Genetics is in the Genetics chapter, or referenced from there. Forensic Pathology is mainly in the Professional Development Chapter.

Patient Management

- This chapter contains aspects of history taking, examination, investigations and management *that don't sit neatly in another chapter*. It therefore focuses on principles and general exam features, and covers some bits and pieces. For specific history taking or examination refer to the relevant chapter.

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History Taking

Frameworks for consultation

- 4 tasks for consultation:
 - Management of presenting problems
 - Modification of help-seeking behaviour (did they come too soon/too late)
 - Management of continuing problems
 - Opportunistic health promotion
- Objective: integration of:
 - Doctor's agenda: Correct diagnosis, preventative health care
 - Patient's agenda: expectations, feelings, fears, understanding of illness experience
- Silverman and Kurtz: - five phases of the consultation:
 - Initiating the session: introduce yourself, why are you here, how can I help (not how are you)
 - Gathering information: start with open questions, physical exam
 - Building the relationship
 - Explanation and planning: what you'll do, what you want the patient to do. Involve patient in planning. Give them as many choices as possible
 - Closing the session: any more questions, check understanding, follow up, emergencies, etc
- Double Diamond model:
 - First phase: patient presents problems, doctor hones down
 - Second phase: diagnosis reached, expansive phase of explanation, management options, then brought to closure
- FIFE: Feelings, Ideas, Function/Dysfunction, Expectations
- Remember: listen, reassure

History Taking

- Always ask why they've come: and why that is a concern to them (what are they scared of?)
- Key skills:
 - Establishing rapport
 - Asking questions in a logical order
 - Observing non-verbal queues
 - Proper interpretation
- Record positive & negative findings. Always amplify positive findings:
 - Time course
 - How quickly did it come on (what were you doing then), pattern since then
 - Site and radiation
 - Character
 - Severity
 - Aggravating or relieving factors
 - Associated symptoms
 - Previous occurrences
- For each potential cause of a symptom think of:
 - Detail of the symptom
 - Other symptoms you would expect if that cause
 - Ask about risk factors of that cause
- See also Talking with Children, page 567 and Talking with Adolescents, page 665

History Outline

- History:
 - Identifying data
 - Presenting complaint (or complaints) eg Cough with green sputum 2 days, Dizziness 4 weeks
 - History of presenting complaint
 - Drug and medication use, including allergies, OTC drugs, herbal/alternative medicines
 - Past medical and surgical history (including hospital admissions)
 - Screen for hypertension, heart disease, asthma, diabetes, epilepsy, rheumatic fever, TB, bleeding tendency, hepatitis B
 - Family history of illness (if genetic illness draw family tree)

- Social history: smoking, alcohol, job, living situation, social supports, overseas travel, functional history in the elderly or disabled
- If a child, then obstetric, neonatal, growth and development, immunisations
- Review of systems
- At end of history always ask ‘is there anything else you want to tell me’
- Note mental function and communication: dementia/delirium common
- Physical Exam:
 - Vital signs: temperature, respiratory rate, pulse, blood pressure
 - General observations: distress, pallor, hydration, cyanosis, weight
 - Relevant systems exams
- Formulation and problem list:
 - List of active problems or clusters of problems (always include smoking if they smoke)
 - List of inactive problems or clusters of problems
 - For each problem, list a set of differential diagnoses, investigations to establish which it is, immediate management, other management strategies
- Progress notes:
 - Changes in symptoms
 - Changes in physical exam or investigation
 - Assessment of what this means
 - Plan for what to do now

Examination

Purpose of Examination

- Aims to:
 - Confirm suspicion
 - Exclude other causes that mimic it
 - Measure severity

General

- Are the conditions OK to do an exam? Is the light in the room OK, is the patient positioned and exposed, etc
- ALWAYS OBSERVE FIRST: stand back and look.
- Distress, comfort, central or peripheral cyanosis, pallor, jaundice, dehydration, SOB, how sick or well
- Cachectic = severe loss of weight and muscle wasting. Usually malignancy, but also severe cardiac disease (due to anorexia from liver congestion and impaired absorption due to intestinal venous congestion)
- Facies: features of the face suggesting diagnoses: eg acromegaly, Cushing’s, Down’s, myxoedema, Parkinson’s, hair distribution in men and women, etc
- Weight, body habitus and posture, including deformities
- Include vital signs in general assessment: pulse, blood pressure, temperature, respiratory rate

Fever

- See also Fever in Children, page 616
- Taking a temperature:
 - Serial measurements the most useful
 - Also take pulse – if ↑temp should have ↑heart rate (except in typhoid)

Normal Values	Low	High
Oral	36.6	37.2
In hot weather	+0.5	+0.5
Rectal	+0.2	+0.5
Axillary	-0.5	-0.5

- Children. The most common emergency presentation in paediatrics. Most common cause is viral infection, otitis media, pharyngitis, and tonsillitis. Also consider bladder infection, Rheumatic fever, Meningitis. Kids spike temperature easily. Febrile convulsions occur between 18 months and 5 years. At other ages investigate other causes

- Types of fever:
 - Continued: does not remit e.g. typhoid, drug fever
 - Intermittent: falls to normal each day – pyogenic infections, lymphomas
 - Relapsing: returns to normal for days then rises again – Malaria, lymphoma, pyogenic

Pyrexia/Fever of Unknown Origin (PYO/FUO)

- See also:
 - Pyrexia of unknown origin if returning from 3rd world, page 511
 - Fever in a Neutropenic Patient, page 301
- Formal definition: > 38 C, > 3 weeks, no known cause (ie normal admission tests already done). However, often used to describe a temperature that you haven't done any tests on yet
- Usually an unusual presentation of a common disease
- History, exam, investigations, time course, urgency and likely cause depend on setting:
 - Community acquired (Classic PUO)
 - Nosocomial PUO (ie hospital acquired)
 - Immune-deficit or HIV related PUO
- Differential:
 - Neoplasm: lymphoma, leukaemia (check lymph nodes), other (hepatic, renal, other)
 - Infection:
 - Bacterial: Tb, abscess (subphrenic, hepatic, pelvic, renal – look for ↑ neutrophils), endocarditis (any dental work?), pericarditis, osteomyelitis, cholangitis, pyelonephritis, PID, syphilis, cystitis
 - Viral: EBV, CMV, HBV, HCV, HIV, Varicella-Zoster
 - Parasitic: malaria, toxoplasmosis
 - Fungal
 - Connective Tissue: RA, SLE, Vasculitis (eg polyarteritis nodosa – check for Raynaud's phenomena – abnormal response in fingers to cold)
 - Miscellaneous: drug fever (especially penicillins, sulphonamides), Rheumatic fever, inflammatory bowel disease, granulomatous disease (eg Sarcoid), Fictitious/Munchausen's (eg injecting themselves with saliva)
- Clues:
 - Weight loss ⇒ chronic
 - Check eyes: iritis in connective tissue disease, jaundice, etc
 - Check tonsils, glands, ears for infection
- History:
 - Travel (eg malaria, did they have prophylaxis)
 - Exposure to others
 - Sexual history
 - Weight loss
 - Been to other doctors (had any antibiotics)
 - Occupational exposure (eg cows)
- Exam:
 - Lymph nodes
 - Heart murmurs
 - Skin for rashes
 - Abdominal exam
- Possible investigations:
 - Blood count
 - Blood cultures
 - Urine microscopy & culture
 - Liver function (eg hepatitis)
 - Viral serology
 - Malaria film
 - Chest X-ray

Tiredness

- Differential:
 - Sleep disturbance: eg anxiety, sleep apnoea, narcolepsy,

- Depression
- Anaemia
- Endocrine: hypothyroidism, hypocortisol (Addison's), diabetes, hypercalcaemia (due to ↑PTH)
- Infection (eg EBV)
- Cancer
- Drugs: alcohol intoxication, sedative drugs,
- Head injury (eg subdural haematoma)
- Post ictal states
- Hypoglycaemia
- Hepatic encephalopathy, Wernicke's encephalopathy
- Chronic heart failure
- Malabsorption (eg coeliac disease)
- Pregnancy
- See also Sleepiness, page 90

Oedema

- Include in exam of appropriate system
- Need to retain 3 – 4 litres before pitting begins
- Exam:
 - Where is it? Distribution
 - Is it pitting
 - Other signs of inflammation
- Mechanisms:
 - ↓colloid osmotic pressure
 - ↑hydrostatic pressure
 - ↓permeability of wall
- Localised Cause:
 - Inflammatory (e.g. infection, allergy - cytokine mediated) → pain/heat/redness/swelling
 - Trauma
 - Venous occlusion by tumour or lymph nodes
 - Thrombosis (e.g. DVT)
- Generalised Cause:
 - Is it bilateral? Usually worse in the evenings
 - Heart Failure:
 - Mechanism: ↑preload → ↑venous pressure, ↓renal perfusion → ↑renin → ↑Na/H2O
 - History: check SOB, orthopnoea, PND
 - Signs/Tests: CXR, ECG, Echo
 - Liver:
 - Mechanism: liver failure/malnutrition → ↓colloid pressure → ↓renal flow → ↑retention
 - History: check alcohol, cholestasis, hepatitis, bleeding, bruising
 - Signs/Tests: portal hypertension, enlarged liver, jaundice, bloods (Liver Function, INR)
 - Renal:
 - Mechanism: nephrotic syndrome → ↓colloid pressure (have to lose 3.5 g protein a day to be nephrotic. NB nephritis is inflammation)
 - History: check change in urination, nocturia (due to diuresis), diabetes
 - Signs/tests: ↑BP, urine test, 24 hr urine, dipstick, urea/creatinine
 - Drugs (eg vasodilators, like calcium channel blockers) can cause ankle oedema
 - Gastrointestinal: Malabsorption → hypoalbuminaemia
- Non-pitting lower limb oedema
 - Lymphoedema (eg malignant invasion of lymphatics, allergy) doesn't pit – push for 10 seconds
 - Hypothyroidism

Hands

- Nails:
 - Takes ~ 6 months for fingernails to grow out
 - Clubbing:
 - Respiratory: carcinoma, fibrosis, cystic fibrosis, TB, chronic suppuration (eg bronchiectasis), idiopathic pulmonary fibrosis, NOT asthma or CORD alone

- Cardiovascular: infective endocarditis
- Other (uncommon): cirrhosis, IBD, coeliac disease, thyrotoxicosis
- Blue: cyanosis, Wilson's disease
- Red: Polycythaemia (red-blue), carbon monoxide poisoning (cherry red)
- Pale nail bed: anaemia
- Koilonychia: spoon shaped nails in Fe deficiency
- Leuconychia: white nails in hypoalbuminaemia
- Mee's lines: single white transverse line in renal failure
- Splinter haemorrhages: usually trauma (especially manual workers) or infective endocarditis, rarely vasulitis (eg in rheumatoid arthritis), polyarteritis nodosa, sepsis, blood malignancy or profound anaemia
- Check capillary refill: squeeze nail and see how long it takes to return to red – sign of peripheral circulation. Normal < 2 sec
- Hands:
 - Palmar erythema: pink spots on pale background – should be bilateral - Chronic liver disease, pregnancy, rheumatoid arthritis, polycythaemia, thyrotoxicosis, SLE
 - Skin: subcutaneous bleeding: petechiae small, purpura bigger, ecymosis – biggest. Petechiae caused by a platelet problem, not due to coagulopathy
 - Dupuytren's Contracture: extend fingers back – shortening of palmar aponeurosis – in alcoholic liver disease, epilepsy, manual workers and idiopathic
 - Asterixis: metabolic flap – coarse, non-symmetrical – neural inhibition → encephalopathy in renal failure (\uparrow urea), respiratory failure (\uparrow CO₂), liver failure (\uparrow nitrogenous material), hypoglycaemia, barbiturate poisoning
 - Raynaud's Syndrome: intermittent attacks of ischaemia of fingers or toes due to intense arterial vasospasm, often precipitated by cold or emotional stimuli
 - Tendon Xanthomata: lipid deposits in tendons of hands or arms in hyperlipidaemia

Head

Headache

- See Headaches, page 139

Eyes

- Jaundice: primary liver disease, liver congestion secondary to heart failure
- Anaemia: pale conjunctiva – especially anterior border just inside eye lid
- Sclera not affected by hypercarotenaemia
- Puffiness below eye: early nephritis (before feet oedema), myxoedema of hypothyroidism

Mouth

- Mouth: Foetor hepaticus, ulceration, pigmentation, telangiectasia, gingivitis/hypertrophy, glossitis
- Ulcers: aphthous, drugs (e.g. gold), trauma, Crohn's, infection (HVZ, HS)
- Pigmentation: heavy metals (lead, iron), drugs (anti-malarials), Addison's, Melanoma, Kaposi's sarcoma
- Snotty nose = coryza

Throat

Bacterial	Viral
High fever	Runny nose
Pus/exudate	Red raw throat
Productive cough (if any)	Persistent dry cough

- Whitish-yellow membrane over tonsils - ?EBV
- Patches of exudate on mucosa - candida
- Differential: Bacterial sore throat, viral URTI, glandular fever, rheumatic fever, quinsy (peri-tonsillar abscess, can lead to airway obstruction)
- See also Acute Pharyngitis, page 63

Lymph Nodes

- Occipital Nodes: scalp infections, bad nits, infected cradle cap, rubella
- Mastoid and posterior auricular

- Parotid: mumps
- Posterior sternomastoid
- Anterior sternomastoid: sore throat
- Jugulodigastric
- Submandibular and Submental: tooth infection, glandular fever
- Superior, deep and lateral cervical (internal jugular) nodes
- Supra & sub-clavicular: lung and lung surface infections, Tb, lung metastasis
- Enlarged lymph nodes and oral thrush → ?AIDS

Investigations

CT and MRI Imaging

- CT:
 - Looks for density ⇒ bones are white (hyper-dense), air is black
 - If it is contrast enhanced then vessels will appear whitish
- MRI (=Magnetic Resonance Imaging):
 - Looks for H atoms
 - Very strong magnet lines up H atoms (effectively little dipoles), radio waves emitted which disturb net magnetic vector, then measure radio frequency emitted by atoms as they return to aligned state
 - Describe as hypo or hyper *intense* – as relates to signal intensity not density
 - Bones on both are black (no free fluid)
 - T1 weighting: simple fluid black (eg CSF, urine). Shows exquisite anatomy
 - T2 weighting: simple fluid turns white. Shows pathology, due to ↑ tissue hydration (eg infection, tumour). T2 shows H₂O. Flowing blood is black

Blood Tests

Why test

- Before ordering any test always ask yourself why you are ordering it. Labs confirm a diagnosis – don't give it
- Diagnosis: to confirm diagnosis/exclude differential diagnosis from history & exam
- Prognosis: severity/progression
- Monitoring: Measure target of treatment rather than drug level (e.g. INR rather than warfarin)
- Screening: Only where test is reliable and you can do something about it

Parameters of a Test

- Normal range: either arbitrary (level which leads to ↓risk) or statistical (what most people are)
- Reliability:
 - Accuracy: mean of test results = real result
 - Precision: variability in results (i.e. want a small standard deviation). Important for serial monitoring. Only different if 2½ SDs from previous test
- Sensitivity: what rate of true positives does it pick up (are all positives found?)
- Specificity: False negative rate
- For further details on sensitivity, specificity, etc, see Sensitivity and Specificity, page 704

Test Results

- Results may be:
 - Real & require interpretation
 - Erroneous: will always be some errors – there should be known rates of error for a lab and these should be within acceptable limits
- Artefact: affected by non-disease factors:
 - Pre-analytical artefacts: mainly at time of collection
 - Incorrect labelling
 - Wrong tube/anticoagulant
 - Haemolysis
 - Delayed transport
 - Temperature effects e.g. refrigerating stuffs up electrolytes
 - Sample incorrectly taken (e.g. through or close to IV lines)

- Pre-analytical factors:
 - Not fasted/wrong time for sample
 - Medications interfere
 - Wrong reference range

Urgent Tests

- If the result may change the immediate management of a patient or if it plays a major role in ongoing assessment of a critically ill patient
- Routine ordering/screening not appropriate in A&E
- Emergency electrolytes:
 - Frequently over-ordered
 - Indications include D/V, seizure of unknown cause, muscle weakness, > 65, known renal/diabetes disease
- Blood gases:
 - Don't need for uncomplicated asthma/MI, or if normal systemic perfusion and no dyspnoea/hyperventilation
 - Indicated if: cyanosis, severe dyspnoea, hypotension, vasoconstricted and sweaty, septic shock, pneumonia, suspected PE, CORD in acute exacerbation
- Beware overdoses: people miscalculate/lie about consumption
 - Timing important: test for paracetamol overdose after 4 hours to judge treatment required. Changes in liver function take 24 hours
 - Ethanol levels: check in unconscious patient, for medicolegal reasons, or if intoxicated but potentially multiple problems
- Toxicology Testing:
 - Serum levels for paracetamol, aspirin, ethanol, methanol, ethylene glycol, lithium, anticonvulsants, digoxin, iron, theophylline
 - Urine screen for drugs of abuse
 - Toxilab screen: long and slow for about 400 therapeutic drugs. Qualitative only
 - Emergency use of cardiac markers: Beware timing - only after 6 hours unless as baseline. Can't size infarcts on cardiac enzymes
- Abdominal pain:
 - Common to find no specific biochemical change
 - Baseline Na, K, creatinine if D/V or surgery likely
 - Amylase, glucose, HCG, LFT, calcium, cardiac enzymes
 - More rarely: urinary porphobilinogen, blood lead
 - Acute pancreatitis may not have ↑ amylase, and ↑ amylase can present in other conditions e.g. perforated/ischaemic bowel, ruptured ectopic pregnancy, diabetic ketoacidosis, renal failure

Treatment

Differential Diagnosis

- Always consider:
 - Autoimmune
 - Degenerative
 - Drugs
 - Doctors
 - Hereditary/congenital
 - Infective
 - Inflammatory
 - Idiopathic
 - Mechanical
 - Metabolic
 - Nutritional
 - Neoplastic
 - Pregnancy
 - Psychiatric
 - Trauma
 - Vascular

Formulating a case

- Differential diagnosis
- What are the risk factors
- Problem list
- Complications of problems and risk factors
- Prognosis: how does this impact on treatment decisions
- Investigations
- Treatment + management/monitoring of side effects
- Integration: stand back and think – am I missing something

Treatment Checklist

- Listen (therapeutic relationship)
- Education
- Lifestyle (diet, exercise, etc)
- Environment/social change
- Psychological
- Drugs
- Surgery
- Referral: to specialists, other health providers, support groups
- Family involvement
- Prevention
- Public Health measures

Behavioural Change

- Health Education is an attempt to achieve behavioural change
- See Parent and Adolescent Education, page 567

Stages of Change Model

- Stages of changes (Prochaska and Di Clemente 1982): Discussion must be tailored to the stage they're at:
 - Pre-contemplation
 - Contemplation
 - Determination
 - Action
 - Maintenance (and maybe permanent exit)
 - Relapse (and maybe return to contemplation)

Readiness to Change/Motivational Interviewing

- Motivation = the probability that a person will enter into, continue and adhere to a specific change strategy. It fluctuates. It is a state not a trait. Measure motivation by what they say not what they do
- Motivational interviewing: goal is to get from the patient their reasons for concern and their arguments for change. Especially helpful in precontemplation/contemplative stages
- Confrontation tends to evoke resistance. Resistance ↓ the chance of change
- Approaches at each stage:
 - Pre-contemplation:
 - Lack of knowledge or inertia
 - Rebellion: try to provide choices
 - Resignation: given up – try to instil hope/explore barriers
 - Contemplation:
 - Not equivalent to commitment
 - Extra information may not make any difference
 - Work through ambivalence, anticipate barriers, ↓ desirability of present behaviour
 - Dealing with ambivalence:
 - “Yes, but...” is normal
 - Helping people resolve ambivalence is key to change
 - Further education may result in conflict or denial
 - Try to get the patient unstuck
 - Poor self-esteem, social context and values may make this difficult

- Highlight discrepancy between personal goals and behaviour. Best if they can identify this discrepancy themselves, rather than feeling pressured
- Motivational Strategies (NB importance of empathy – understanding where the patient is at):
 - A – give Advice
 - B – remove Barriers
 - C – provide Choices
 - D – decrease Desirability: alter balance of perceived costs, barriers and rewards
 - E – practice Empathy. Accept and understand without agreeing
 - F – provide Feedback
 - G – clarify Goals
 - H – active Helping
- Counselling techniques:
 - Open ended questions
 - Reflective listening: voice what you think the patient means by what they are saying
 - Affirm: ↑ self esteem and support the patient
 - Summarise

Brief Interventions in General Practice

- Brief but repeated interventions avoid stigmatism, and are more effective than one long session
- Direct advice normally provokes resistance
- Opening lines:
 - “What are some good things about.... What are the less good things...”
 - Ask permission before giving information: “I wonder, would you be interested in knowing more about”. When you’ve finished: “What do you make of all this?”
 - “What concerns do you have about ...”

Breaking Bad News

- Prepare patient for what is to come – give an honest explanation of why you’re doing investigations before you do them
- Think ahead – invite family members when results come back
- If there is no family, take a nurse (who has probably been preparing them anyway)
- Ask patient what they understand is happening or what they’re scared of – gives you a good intro
- It is the patient’s information – let them decide the pace and level of detail
- If the patient asks ‘have I got cancer’ then they will have been thinking about it and will have a reason for asking – this is helpful
- If the patient asks ‘What do you think’ then they’re likely to be anxious. Need to open up discussion and give them opportunity to express their fears
- Break up the information – ‘chunk and check’. Check understanding bit by bit
- ‘Denial’ can be shock, disbelief, or failure to understand. Denial is a longer-term pattern of behaviour. Whether denial is bad or not depends on the consequences
- Document your discussion and what you’ve said

Cardiovascular

- See also Heart Disease in Children, page 596
- References: Prof Delahunt's Pathology Notes

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Physiology and Anatomy

Physiology

- Cardiac Output (CO):
 - CO = MAP/TPR (ie flow = pressure / resistance)
 - CO = SV * HR
 - Normal adult at rest = 5 L/min
 - Can be measured with Doppler/echo
- Mean Arterial Pressure:
 - MAP = Cardiac Output*TPR
 - MAP = Diastolic + 1/3(systolic-diastolic)
- Stroke volume:
 - SV = End diastolic volume – end systolic volume
 - Normal 60 – 80 ml
- Ejection fraction = ESV/EDV. Determined by:
 - Preload (=EDV): dependent on blood volume, venous tone, posture, intrathoracic pressure, peripheral muscle pump, and atrial contraction (20% of filling). Affects stroke volume through Starling's Law: ↑myocardial fibre length (ie filling) → ↑SV until ventricle is over-stretched. Can be measured for the left ventricle using pulmonary artery/capillary wedge pressure (CAWP) and for the right using central venous pressure
 - Force of Contraction (Inotropy): Shifts Starling Curve up and to the left. Increased by sympathetic stimulation, ↑Ca, ↑thyroxine, ↑angiotensin, drugs, ↑temp, ↑HR. Decreased by acidosis, hypoxaemia, ↑K, drugs (general anaesthetics, beta blockers)
 - Afterload = tension in the ventricular wall at the end of systole. Results from ventricular distension, elasticity of arterial walls and arterial network resistance. Measure with arterial catheter
 - Changes given certain shock states:

Cause	CVP	PAWP	BP	HR	Urine Output
Blood Loss	↓	↓	↓	↑	↓
L V Failure	↑	↑	↓	↑	↓
R V Failure	↑	↓	↓	↑	↓
Fluid overload	↑	↑	↓	↑	↑

- Peripheral vascular resistance:
 - Resistance proportional to radius to the power of 4
 - = (Mean aortic pressure – right atrial pressure)/cardiac output

Cardiac Anatomy

- Heart Valves:
 - Mitral valve (left AV): anterior and posterior leaflets
 - Tricuspid valve: anterior, posterior and septal cusps
 - Aortic valve: left, right and posterior cusps
 - Pulmonary valve: left, right and anterior cusps
- Blood supply:
 - Left main stem (LMS) → LAD (anterior wall of LV and anterior 2/3 of septum) and Circumflex (lateral wall of left ventricle and most of the posterior wall of the LV). Also supplies AV node, and SA node in 60%
 - Right coronary artery → right atrium, right ventricle (except for left part of anterior wall), right posterior and inferior walls of LV and posterior 1/3rd of septum
- Pericardial effusion: normal content of pericardial sac = 50 ml. Effusion can be serous, chylous or haemorrhagic. Sign of pericarditis but also accompanies MI

Regional Blood Flow

Organ (mass)	% Of Cardiac Output	O ₂ consumption (ml/100g/min)	Regulation of blood flow
Heart – 300 g	5% - 250 ml/min	10	Metabolites (CO ₂ , K, H, lactate, adenosine); α & β adrenergics
Kidneys – 300 g	20 % - 1000 ml/min	6	Myogenic autoregulation, angiotensin, α adrenergics, PGs, juxta-glomerular feedback
Brain – 1500 g	15% - 750 ml/min	3	H ⁺ ; myogenic mechanisms
Liver – 2500 g	30% - 1500 ml/min	2	MAP, portal blood flow (local metabolites), adrenergics
Muscle – 35 kg	15% - 750 ml/min	0.2	α & β adrenergics; local metabolites (K ⁺)
Skin – 3500 g	10% - 500 ml/min	0.2	α adrenergics; kinins (thermoregulation); axonal reflex; sympathetic cholinergic

- Cerebral Perfusion:
 - Cerebral blood flow (CBF) = [MAP – ICP (or CVP, whichever is greatest)]/cerebral vascular resistance
 - Minimal desirable perfusion pressure is 60 mmHg. This is reduced by ↓arterial pressure, ↑venous pressure, constriction/spasm of cerebral vessels or ↑intra-cranial pressure (ICP)
 - Autoregulation keeps CBF at 50 ml/100g/min. Less than 15 → changes in electrical activity
- Coronary Perfusion:
 - Perfused during diastole
 - Coronary perfusion = (Mean diastolic pressure – VEDP)/Coronary Vascular Resistance
 - So treat poor perfusion with:
 - High diastolic pressure (eg systemic vasoconstrictor - α agonist)
 - Reducing end diastolic ventricular volume (prevent volume overload)
 - Decrease coronary vascular resistance (eg coronary vasodilator)
 - Slow heart rate → longer diastolic phase (eg beta blockers)
 - ↓Preload (nitrates and Ca channel blocker)
 - O₂ therapy and maintain haemoglobin
- Renal Perfusion:
 - Normally autoregulated down to 80 mmHg systolic. When BP ↓, renal blood flow ↓↓ → renal failure and acute tubular necrosis
 - Treatment:
 - Colloid/saline → ↑BP
 - Dopamine 2 – 5 mg/kg/min → ↓renal vascular resistance

History

- Major symptoms:
 - Chest pain/heaviness/discomfort
 - SOB (exertional, orthopnoea, PND)
 - Ankle swelling
 - Palpitations (due to ↑EDV, or do they mean arrhythmia – usually sudden onset – or tachycardia – usually gradual onset)
 - Syncope
 - Intermittent claudication (pain in legs on exertion due to ischaemia)
 - Fatigue
- Key differentials:
 - Does it change with breathing? (\Rightarrow ?respiratory cause)
 - Does it change with movement or localised pressure (\Rightarrow ?musculoskeletal cause)
 - Past history screen: Rheumatic fever, STDs, recent dental work, thyroid disease, history of heart disease, drugs
 - Social history: tobacco (ask ‘have you ever smoked’ not ‘do you smoke’ just in case they ‘gave up this morning’), alcohol, occupation
 - Family history: Ischaemic heart disease, valve disease, congenital disease, Marfan’s

- Risk factors of Coronary Artery disease: hyperlipidaemia, smoking, hypertension, family history, diabetes mellitus, obesity, ↓exercise, male, advanced age

Differentiating Chest Symptoms

Cough

- Due to non-specific irritation from pharynx to lungs
- Note duration:
 - Short ⇒ Respiratory tract infection (especially if fever)
 - Long ⇒ asthma, CHF
 - Long + irritating and dry ⇒ ?reflux and aspiration
 - Long + sputum ⇒ bronchiectasis
- Note time of day:
 - Night ⇒ asthma, heart failure
 - After food ⇒ reflux
- Infective respiratory causes:
 - Yellow/green sputum ⇒ bronchitis, pneumonia
 - Dark, fowl smelling sputum ⇒ anaerobic abscess
- Other potential causes:
 - CORD
 - Psychogenic
 - ACE inhibitors
- Sputum:
 - Yellow or green: lobar pneumonia or bronchiectasis
 - Foul smelling and dark: anaerobic abscess
 - Pink and frothy: not sputum but pulmonary oedema
- Haemoptysis (coughing blood) can be: bronchitis, cancer, bronchiectasis, cystic fibrosis, abscess, pneumonia, TB, foreign body, Goodpasture's syndrome, rupture of a blood vessel after coughing, LV failure or mitral stenosis. Exclude nasal bleeding and haematemesis

Chest Pain

- Very common reason for A & E attendance: but only a few have S-T elevation MI
- Very localised pain (i.e. point to it with a finger) unlikely to be ischaemic
- History taking:
 - Often a lot of denial
 - Key question is time course (acute & on-going, episodic, persistence, etc)
 - What causes it? If exertion, how far can you walk? Worse going up hill or into a cold wind? How long does it take to settle? What do you do to relieve it? Is the pain related to breathlessness
 - Family history: not when did family die but when did it start – if patient young then looking for early onset in family
 - Risk factors: smoking, hypertension, diabetes, hyperlipidemia, obesity, homocystinaemia, age, sex (women better prior to menopause).
- Causes:
 - Cardiac:
 - Myocardial ischaemia (narrowing of arteries, acute thrombosis, stenosis → ↓perfusion pressure, angina pectoralis). Gripping, crushing central chest pain. Pain may radiate. Provoked by exercise, relieved by rest
 - Myocardial infarction
 - Pericarditis (if infectious then severe inflammation, if secondary to MI then more mild. ST elevation on *all* leads). Pain changes with position/movement, respiration & coughing. Sharp & severe central chest pain
 - Aortic Stenosis
 - Vascular:
 - Aortic aneurysm: central chest pain radiating to the back. Can mimic MI pain
 - Pulmonary Embolism (PE): very sudden onset of SOB – may ease gradually (as clot disperses). Several days later – pleuritic chest pain, *may* have high fever, haemoptysis
 - Dissection: brachial pulse in each arm different, very sudden onset of very severe pain (c.f. MI has unstable angina phase first)

- Right ventricular strain
- Pulmonary:
 - Pleuritis or Pneumonia
 - Tracheobronchitis
 - Pneumothorax
 - Tumour
 - Emphysema
- Gastrointestinal:
 - Oesophageal reflux
 - Oesophageal spasm
 - Mallory-Weiss tear
 - Peptic disease (injury to oesophagus, ulcers, pancreatitis, biliary)
 - Biliary disease
 - Pancreatitis: do amylase to exclude
- Musculoskeletal (will be localised – can point to it, will be palpable tenderness, pain on movement and maybe history of trauma)
 - Cervical disk disease
 - Costochondritis
 - Arthritis of shoulder or spine
 - Intercostal muscle cramps
 - Subacromial bursitis
- Other:
 - Breast disorders
 - Chest wall tumours
 - Herpes Zoster prior to eruption
 - Psychogenic causes

Breathlessness

- Normal up to 16 breaths per minute. 20 is definitely high
- History questions should include:
 - Ask patient what they mean by breathless
 - How much exertion does it take to make them breathless (eg distance walked, stairs climbed)
 - Exclude obesity and lack of fitness
 - Chest pain: pleuretic is sharp and made worse by coughing and deep inspiration. Usually localised
 - Occupational triggers: e.g. asbestos, legionella, occupational allergens, hobbies, birds, animals
 - Onset (slow over years⇒ ?fibrosis)
 - SOB on raising arms (eg reaching into a cupboard) ⇒ using accessory muscles to breath
 - Orthopnoea: breathless when lying down
 - Fever at night: consider TB, pneumonia, mesothelioma
 - Sleep apnoea: ask about snoring, daytime somnolence, chronic fatigue
 - Anxiety symptoms
 - Immune status (→ PCP or TB)
 - Medications for clues to condition and for possible side effects, eg PE from OC pill, cough from ACE inhibitors, cocaine
 - SMOKING
- Check: cyanosis, can they complete a sentence, peak flow, consciousness level, pulse
- Divide into:
 - Acute: PE, hyperventilation (tingling, strange pains – alkalotic), acute LVF (no oedema c.f. CHF), pneumothorax, lung collapse due to many causes, pneumonia
 - Chronic: COPD (asthma, bronchitis, emphysema), interstitial lung disease
 - Asthma is fluctuating not progressive (i.e. ‘Do you have good days and bad days?’)
 - Obstructive: trouble breathing out
 - Restrictive: trouble breathing in
 - Think of systems: cardiac, respiratory, blood (anaemia, jaundice), hyperthyroidism, psychogenic, acidosis etc
 - Paroxysmal Nocturnal Dyspnoea (PND):
 - Paroxysmal = sudden recurrence or intensification of symptoms

- Heart failure: wakes feeling like they're suffocating, get out of bed and open window, may wheeze (cardiac asthma), may take $\frac{1}{2}$ an hour to settle
- Sleep apnoea: wakes feeling like they're suffocating, panics, sits up, and settles very quickly. Get collaborative history
- Asthma: wakes up coughing

Cyanosis

- Caused by > 50 gm/L of reduced Hb (so if \uparrow Hb concentration and CORD then easy to be cyanosed → blue bloaters)
- $< 66\%$ saturation at normal HB (ie late sign)
- $< 40\%$ saturation in anaemia
- Causes:
 - Cardiac: shunts or congenital heart disease
 - Non-cardiac: e.g. hypoxia

Physical Exam*

- Position patient at 45 degrees
- General appearance, including cachectic state, Marfan's, Down's or Turner's Syndromes
- Dextrocardia = heart on right hand side (1 in 400??). Need right-sided heart leads

Peripheral Exam

Hands

- Check for clubbing (congenital cyanotic heart disease), warmth (perfusion), capillary refill, anaemia (palmar creases), peripheral cyanosis, splinter haemorrhages

Pulse

- Radial pulse: assess rate, rhythm, and delay from radial to femoral pulse (radio-femoral delay)
- Brachial or Carotid pulse: Character and volume
- Rate:
 - Sinus Tachycardia:
 - = Sinus rhythm > 100 bpm. 120 bpm could be physiological, $> 140 - 150$ bpm more likely to be an aberrant rhythm
 - Causes: fever, exercise, emotion, anxiety, pain, pregnancy, anaemia, hypoxia, thyrotoxicosis, HF, catecholamine excess, constrictive pericarditis, myocarditis, shock, MI, drugs, smoking, coffee, autonomic neuropathy (eg in DM), PE
 - Sinus bradycardia:
 - = Sinus rhythm < 60 bpm
 - Causes: athlete, during sleep, drugs (β -blockers, digoxin, amiodarone), hypothyroidism, hypothermia, severe jaundice (due to bilirubin in conducting system), 3rd degree heart block, MI, paroxysmal bradycardia (eg vasovagal syncope)
- Rhythm:
 - Regular
 - Irregular:
 - Irregularly irregular: usually atrial fibrillation
 - Regularly irregular: Sinus arrhythmia (rate \uparrow with respiration and \downarrow with expiration) or 2nd degree heart block (Mobitz type 1)
- Quality:
 - If 'thin' then \downarrow volume
 - Slow rising, low volume ⇒ aortic stenosis
 - Radial/femoral delay ⇒ aortic stricture e.g. coarctation,
 - Bounding pulse = a pronounced pulse – big difference between systolic and diastolic pressure (i.e. large pulse pressure). If bounding then always do a collapsing check
 - Collapsing pulse = bounding pulse + thumping pulse felt over wrist with palm of your hand when patient's arm raised - ?aortic regurgitation (higher column of blood → \uparrow regurgitation)
- Pulse deficit = difference between the radial pulse rate and heart rate. If rapid or irregular contraction then no time for ventricular filling ⇒ there may not be a corresponding radial pulse beat

Measuring Blood Pressure

- Ways of measuring blood pressure:
 - Mercury sphygmomanometer: listen for Kortokoff sounds
 - Oscillotonometer: detects arterial pulsations transmitted by the cuff. Tend to over-read very low pressures (oscillations diminish in amplitude)
 - Ultrasound sphygmomanometer: uses Doppler shift
 - Direct measurement: intra-arterial pressure with transducer
- How to measure with a sphygmomanometer:
 - Patient relaxed/seated for 5 minutes
 - Arm at heart level
 - Hold their hand under your right arm, straighten their arm and support under elbow. Use right thumb to feel brachial pulse as cuff is inflated (so you don't over-inflate). Inflate to 30 mmHg above point where pulsation stops
 - Don't push stethoscope diaphragm too hard (otherwise → bruit)
 - Start of Kortokoff sound 1 = systolic. Disappearance of Kortokoff sound 5 = diastolic
 - In obese people a normal width cuff will over-estimate blood pressure – must use a large one
 - Repeat several times, and on several occasions before deciding to treat
 - Sources of operator error:
 - Wrong sized cuff
 - Poor positioning of the patient
 - Too rapid release of cuff pressure
 - Use of non-standard diastolic end points
 - Rounding to 5's or 10's
- Watch for:
 - Pulsus paradoxus: Normally inspiration → ↓systolic and diastolic blood pressure (more negative intrathoracic pressure → pooling in pulmonary vessels → ↓filling). Pulsus paradoxus = this decrease is exaggerated (ie fall of > 10 mmHg). Can occur in constrictive pericarditis, pericardial effusion or severe asthma
 - Postural hypotension:
 - Fall of more than 15 mmHg systolic or 10 mmHg diastolic on standing
 - Causes: hypovolaemia, drugs (vasodilators, antidepressants, diuretics), Addison's disease, hypopituitarism, autonomic neuropathy
 - ↑Pulse on standing. For vasovagal syncope pulse ↓
- See also Hypertension, page 34

Face

- Eyes:
 - Jaundice from liver congestion secondary to heart failure
 - Anaemia
 - Roth's spots on retina: areas of retinal infarction and haemorrhage caused by septic emboli in bacterial endocarditis
- Xanthelasma: intracutaneous yellow cholesterol deposits around the eye. Normal variant or ?hyperlipidaemia
- Mitral facies: rose cheeks with dilated blue veins and cyanosed tongue. Due to pulmonary hypertension and ↓cardiac output (eg as in severe mitral stenosis)
- Mouth: diseased teeth (cause of infective endocarditis), tongue for central cyanosis, and mucosa for petechiae

Carotid Arteries

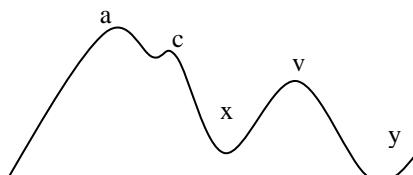
- Never palpate both at once → occlude blood supply to brain
- Information about aorta and left ventricular function

- Pulse wave forms:

Type	Causes
Anacrotic: small volume, slow uptake	Aortic stenosis
Bisferiens: anacrotic and collapsing	Aortic stenosis and regurgitation
Collapsing	Aortic regurgitation, hyperdynamic circulation (eg exercise, fever), patent ductus arteriosus, atherosclerotic aorta
Small volume	Aortic stenosis, pericardial effusion
Alternans: alternating strong and weak beats	Left ventricular failure
Jerky	Hypertrophic cardiomyopathy

Jugular Venous Pressure (JVP)

- Information about right atrial and right ventricular function
- ↑ in RVF, volume overload, impaired RV filling, SVC syndrome
- Positioning:
 - Patient should be at 45 degrees
 - Internal jugular is medial to the superior end of sterno-mastoid then runs behind it as it descends
 - External is lateral, is easier to see, but is more tortuous and therefore less reliable
 - Sternal angle is the zero point – pulsations are visible above this point at 45 degrees (centre of the right atrium is 5 cm lower). Normal is pulsations just above the clavicle (+3 cm)
- Differentiating from carotid pulse. The JVP is:
 - Visible but not palpable
 - Flickers twice with each cardiac cycle
 - Usually decreases with respiration
 - Is obliterated then filled from above following light pressure at the base of the neck
- Pressure waves in atria:



- a wave: atrial contraction at end of diastole → ↑ atrial pressure. Coincides with first heart sound and precedes carotid pulse. Closely followed by ...
- c point: bulging of AV valves into atria during systole → ↑ atrial pressure. Not usually visible
- x descent: atrial relaxation between S1 and S2
- v wave: End of atrial filling during systole – venous inflow into atria with AV valve closed → ↑ atrial pressure
- y descent: rapid ventricular filling following opening of the AV valve
- Height (the easy bit – ha ha!):
 - If > 3 cm above the zero point then right heart filling pressure is raised
 - Rises with 10 seconds pressure on the liver (hepatojugular reflex). A rise is normal. If it remains raised then ventricular failure
 - Causes of ↑ height: Right ventricular failure, tricuspid stenosis or regurgitation, pericardial effusion or constrictive pericarditis, SVC obstruction (no waves), fluid overload, hyperdynamic circulation
 - Should normally fall on inspiration. If it rises then ?constrictive pericarditis. Investigate with echo
- Character (the hard part):
 - Causes of a dominant a wave: tricuspid stenosis (also causes a slow descent), pulmonary stenosis, pulmonary hypertension
 - Causes of cannon a waves (↑↑wave - right atrium contracts against closed tricuspid valve): intermittently in complete heart block (two chambers beating independently), retrograde conduction
 - Cause of dominant v wave: tricuspid regurgitation (should never miss this, watch for movement of ear lobe)
 - x descent: absent in AF, exaggerated in cardiac tamponade, constrictive pericarditis

- y descent: Sharp: severe tricuspid regurgitation, constrictive pericarditis, slow in tricuspid stenosis, right atrial myxoma

Praecordium

Inspection of the Praecordium

- Scars:
 - Median sternotomy: any surgery requiring cardiopulmonary bypass
 - Left lateral Thoracotomy: ?closed mitral valvotomy
- Note structural abnormalities: Pectus excavatum (sunken chest = funnel chest) or kyphoscoliosis may distort position of heart and vessels (ie shifting the apex beat). If severe then ↓pulmonary function
- Note presence of pacemaker
- Pulsations: apex beat and others (eg over pulmonary artery in severe pulmonary hypertension)

Palpation of the Praecordium

- Apex beat:
 - Count down intercostal spaces (the 2nd space is the first one palpable, opposite the sternal angle). Find most lateral and inferior point at which pulsations are felt
 - Normal = 5th intercostal space, mid-clavicular line
 - If not palpable then thick chest wall, emphysema, pericardial effusion, shock (or rarely dextrocardia – inversion of heart and great vessels onto right side)
 - Pressure overloaded = systolic overloaded: Forceful, sustained, not displaced. Due to hypertension, aortic stenosis
 - Volume loaded = diastolic overloaded = hyperkinetic: displaced, unsustained, uncoordinated, large area. Due to aortic or mitral regurgitation, dilation, LV dysfunction (eg anterior MI)
 - Double or triple impulse = hypertrophic cardiomyopathy
- Parasternal impulse: heel of hand rested just to the left of the sternum. Feel movement with systole in right ventricular enlargement or severe left atrial enlargement (right ventricle pushed anteriorly)
- Tap of pulmonary valve closure (P2) over pulmonary areas in pulmonary hypertension
- Thrills = palpable murmurs. Apical thrills felt best with patient rolled onto left side. Pulmonary or Aortic thrills best felt with patient sitting up, leaning forward and on expiration. A thrill coinciding with the apex beat is a systolic thrill, otherwise a diastolic thrill

Percussion of the Praecordium

- A waste of time!

Heart sounds

- Stethoscope head:
 - Bell: good for low pitched sounds, eg diastolic murmur (mitral stenosis) or 3rd heart sound. Don't press too hard otherwise skin becomes a diaphragm
 - Diaphragm: good for high pitched sounds, eg systolic murmur or 4th heart sound
- Using stethoscope, auscultate:
 - Mitral area (4th intercostal space, left mid-clavicular line) with bell and diaphragm
 - Tricuspid area (5th intercostal space, left sternal edge) with diaphragm
 - Pulmonary area (second intercostal space, left sternal edge) with diaphragm
 - Aortic area (second intercostal space, right sternal edge) with diaphragm
- Heart Sounds:
 - First heart sound: closure of mitral and tricuspid valves at beginning of systole. Mitral closes slightly before tricuspid but you won't hear the difference
 - Second heart sounds: closure of aortic and pulmonary valves. Lower pitch. End of systole. Aortic closes first (higher back pressure on valve) → splitting of heart sounds. But pulmonary closure is not heard over all the praecordium, so splitting best heard over pulmonary area. Inspiration → ↑venous return → later closure of pulmonary valve → enhanced splitting
 - Use carotid pulsation to orientate to timing. This occurs during systole, between S1 and S2

Abnormal Heart Sounds

S1	Loud	Mitral or Tricuspid Stenosis → limited ventricular filling → no easing of low at end of filling → valves snap shut. Also ↓diastolic filling (eg in tachycardia)
	Soft	Prolonged filling (eg 1 st degree heart block) or failure of leaflets to close properly (eg mitral regurgitation), delayed LV systolic (eg LBBB)
	Splitting	Most often due to right bundle branch block
S2	Loud	Loud aorta in patients with hypertension and congenital aortic stenosis (→ forceful closure). Pulmonary closure loud in pulmonary hypertension
	Soft	Aortic calcification or regurgitation → leaflets don't close well
	Increased Splitting	If abnormal ⇒ delay in right ventricular emptying, eg right bundle branch block, pulmonary stenosis, pulmonary hypertension, ventricular septal defect (→ ↑right ventricle filling). Also mitral regurgitation → earlier aortic valve closure
	Fixed splitting	Doesn't change with respiration ⇒ atrial septal defect and both atria have equal volumes
	Reversed splitting	P2 occurs before A2, and gap increases on expiration. Due to delayed left ventricular emptying (left branch bundle block, severe aortic stenosis, coarctation of the aorta, or large patent ductus arteriosus)

Extra Heart Sounds

	Description	Cause
S3	Low-pitched mid-diastolic sound. Called Gallop Rhythm	?Caused by tightening of mitral or tricuspid muscle at the end of rapid ventricular filling. Normal in children and young people. Pathological when ↓ ventricular compliance, so get S3 even when filling is not rapid
Left Ventricular S3	Louder at apex than at sternal edge, and louder on expiration	Normal under 40 years and in pregnancy. Otherwise, left ventricular failure, also aortic regurgitation, mitral regurgitation, ventricular septal defect and patent ductus
Right Ventricular S3	Louder at sternal edge than apex, and louder with inspiration	Due to right ventricular failure of constrictive pericarditis
S4	Late diastolic sound, higher pitched than S3. Can sound like a gallop rhythm.	Always abnormal. Due to high-pressure atrial wave reflected back from a poorly compliant ventricle. Doesn't occur in AF as it requires atrial contraction
Left Ventricular S4	Often during angina or MI	↓ Left ventricle compliance: aortic stenosis, acute mitral regurgitation, systemic hypertension, ischaemic heart disease, age
Right Ventricular S4		↓ Ventricular compliance: pulmonary stenosis or pulmonary hypertension
Summation Gallop	If the heart rate > 120 bpm, S3 and S4 may be superimposed, and therefore more audible	Only implies ventricular stress if S3 or S4 persists when heart rate slows

Miscellaneous Sounds

- Opening Snap: High-pitched sound after S2 in mitral stenosis, due to sudden opening of the mitral valve. Don't confuse with widely split S2 (snap is higher pitched)

- Systolic ejection click: early systolic high-pitched sound over aortic or pulmonary areas. Is caused by pulmonary or aortic congenital stenosis and is followed by a systolic ejection murmur
- Non-ejection systolic click: high pitched systolic sound over the mitral area. Common. May be followed by systolic murmur. Due to mitral prolapse and atrial septal defects
- Diastolic pericardial knock: may occur if there is a sudden cessation of ventricular filling in constrictive pericardial disease

Heart Murmurs

Timing of Murmurs

Murmur	Nature	Cause
Pan systolic	Pan-systolic: extend from S1 to S2, loudness and pitch vary during systole	Ventricular leakage: Mitral or tricuspid regurgitation, ventricular septal defects
Ejection (mid) systolic	Intensity greatest in early to mid-systole then wanes	Turbulent flow through an orifice: Aortic or pulmonary stenosis, hypertrophic cardiomyopathy, atrial septal defect
Late systolic	Noticeable gap between S1 and murmur, and continues to S2	Mitral valve prolapse or papillary muscle dysfunction
Early Diastolic	Begins with S2 and fades (decrescendo). High pitched.	Regurgitation through a leaky valve: Aortic or pulmonary regurgitation.
Mid Diastolic	Begin after S2, may extend to S1. Lower pitched.	Impaired flow during filling: Mitral or tricuspid stenosis
Pre Systolic	Just before S1	Atrial systole increases blood flow across the valve: Mitral or tricuspid stenosis
Continuous murmurs	Through systole and diastole	Communication where there's a permanent pressure gradient: Patent ductus, numerous malformations or fistulas
Combined systolic and diastolic murmurs		Aortic stenosis and aortic regurgitation
Pericardial friction rub	Superficial scratching sound at any time in the cycle. Intermittent. May varies with respiration and posture	Pericarditis

Listening for Murmurs

- Areas of greatest intensity: Mitral regurgitation is loudest over the apex and radiates into the axilla – but may be heard over the whole praecordium. Aortic murmurs radiate into the carotid arteries
- Benign murmur of pregnancy – ejection systolic. Pan systolic or diastolic murmurs are abnormal
- In general, systolic murmurs are easier to hear than diastolic murmurs
- Loudness: Doesn't always correlate with severity but a change is significant (eg after an MI).
 - For systolic:
 - Grade 1/6: very soft. Consultants only!
 - Grade 2/6: soft. Detected immediately by an experienced operator
 - Grade 3/6: moderate but no thrill
 - Grade 4/6: loud, thrill just palpable
 - Grade 5/6: very loud, thrill easily palpable
 - Grade 6/6: audible without stethoscope
 - For diastolic: Usually graded 1 to 4
- Pitch: low pitched \Rightarrow turbulent flow under pressure (eg mitral stenosis), high pitched \Rightarrow high velocity (eg mitral regurgitation)

- Clues can also be obtained from peripheral signs (eg tricuspid regurgitation → pulsatile liver, slow rising pulse → aortic stenosis)
- Dynamic manoeuvre testing:
 - Respiration: Right sided murmurs louder on Inspiration (due to ↑venous return), Left sided louder on Expiration (brings heart closer to the chest wall – especially for aortic regurgitation) – RILE
 - Valsalva manoeuvre (↓preload): Hold nose, close mouth, breathe out hard to pop ears and hold. Listen over left sternal edge for changes in the systolic murmur of hypertrophic cardiomyopathy, and over the apex for mitral valve prolapse. Other murmurs will be quieter due to ↓left and right filling
 - Squatting or leg raise (↑preload): ↑venous return and ↑arterial resistance → most murmurs are louder
 - Handgrip (↑afterload): aortic stenosis quieter

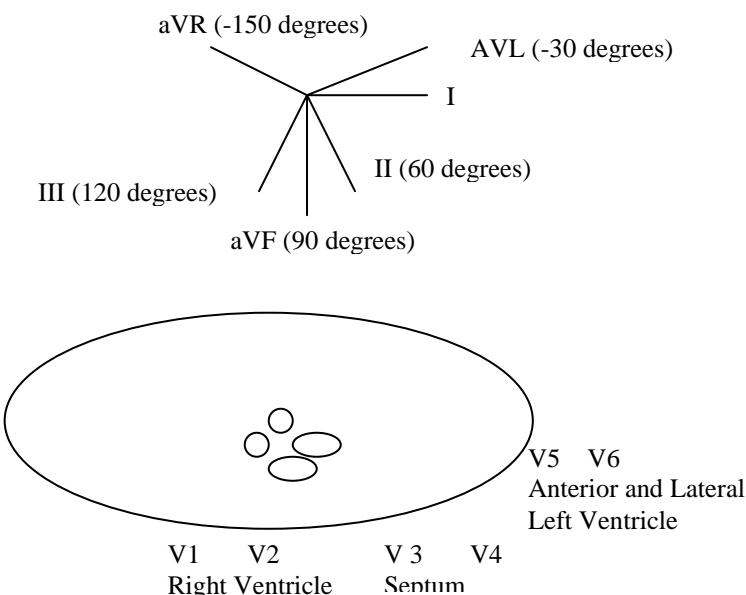
Lungs, Abdomen and Legs

- Percuss and auscultate lung bases on the back for pulmonary oedema, then check for sacral oedema
- Abdomen:
 - Tender or enlarged liver ⇒ ?heart failure
 - Pulsatile liver ⇒ ?tricuspid regurgitation
 - Ascites ⇒ ?heart failure
 - Splenomegaly ⇒ ?infective endocarditis
- Legs:
 - Femoral artery pulses: palpate and auscultate for bruits
 - Popliteal pulse
 - Feel leg pulses both sides at once, standing at end of bed (gives you two chances to find them!):
 - Posterior tibial pulse: posterior to medial malleolus
 - Dorsalis pedis pulse: just lateral to the extensor hallucis longus tendon (seen when big toe dorsiflexed)
 - Palpate the distal shaft of the tibia for oedema – press for 15 seconds. If present, note upper level
 - Cyanosis and clubbing of the toes, pallor, cool, ↓capillary refill of toes

ECG Interpretation*

- Reference: ECG Made Easy, J R Hampton, Churchill Livingston, 1997. Well worth a read
- 5 mm (one large square) = 0.2 secs ⇒ 300 squares per minute

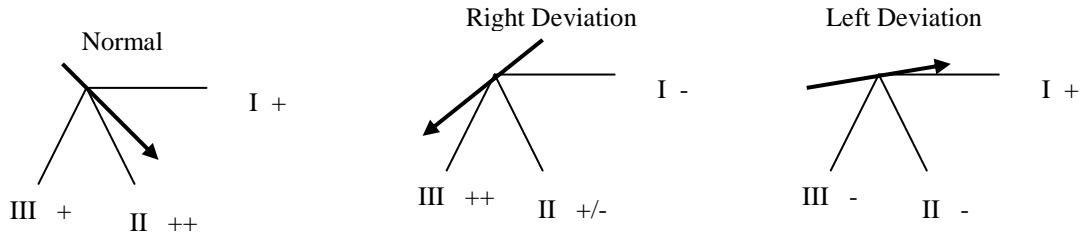
Leads



- Depolarisation:
 - R > S: depolarisation spreading toward lead
 - R < S: depolarisation spreading away from lead

- R = S: depolarisation at right angles to lead

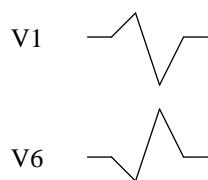
Axis



- To check axis, look at I, II and III. Normal is between VL and VF
- Alternative: cardiac axis is at right angles to lead in which R & S are the same size
- Right Deviation: ?hypertrophy of RV or tall and thin.
- Left deviation: ?hypertrophy of LV

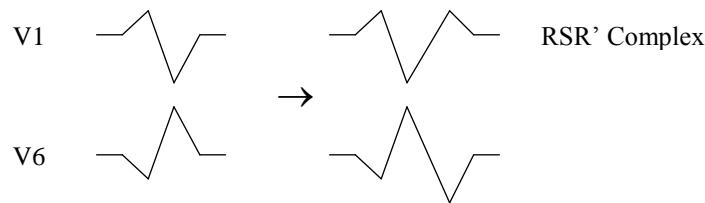
QRS Complex in V Leads

- Shape is determined by:
 - Septum is depolarised first, and the wave spreads from L to R in the septum:
 - V1 initially up as depolarisation in the septum ($L \rightarrow R$) is towards the lead
 - V6 initially down as depolarisation in the septum is away from lead
 - Muscle mass: LV dominates so V1 is down and V6 is up.

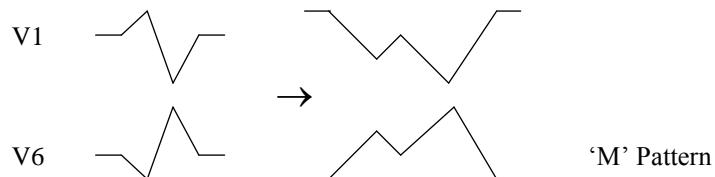


Bundle Branch Block

- Delay in depolarisation of part of the muscle \rightarrow widened QRS. If QRS $>$ 3 small squares (0.12 secs) \Rightarrow slowed conduction \Rightarrow bundle block *or* ventricular ectopic beat.
- Right Bundle Branch Block (Can be benign. ?Atrial septal defect): Left depolarises first, then right. May just be delay to the terminal end of QRS (especially in V5)



- Left Bundle Branch Block. Always pathological. RV depolarises, then wave spreads to LV. T wave inversion in anterior and lateral leads is common (I, VL, V4 – V6). Wide QRS



- Left bundle divides into the anterior and posterior fascicles. Failure of the anterior fascicle \rightarrow left axis deviation (depolarisation is through the posterior fascicle)
- If LBBB: ?aortic stenosis, ischaemic disease
- To determine side of block: W in V1 and M in V6 is Left (WiLLiam). M in V1 and W in V6 is Right (MaRRRow). *LBBB prevents any further interpretation of the ECG*

Reporting an ECG

- Check **rate**: bradycardia or tachycardia?
- Check **rhythm**:

- See also Arrhythmias, page 39
- Regular or irregular
- Sinus rhythm = one P wave per QRS complex \Rightarrow depolarisation begins in SA node.
- Sinus arrhythmia:
 - Bradycardia: athletes, fainting attacks, hypothermia, myxoedema, drugs
 - Tachycardia: exercise, fear, pain, shock, thyrotoxicosis
- Supraventricular arrhythmia:
 - = Sinus, atrial or junctional/nodal arrhythmia
 - QRS is normal width (unless also bundle block)
 - Escape beats are atrial, nodal or ventricular pacemakers that fire if the SA node fails, as they have a slower intrinsic rate. Escape beats come late.
 - Atrial escape: abnormal P wave after SA node fails. Normal QRS
 - Nodal escape: no P wave (either none or buried in Normal QRS)
 - [Ventricular escape – not supraventricular: usually in complete heart block. Fast P waves. Slow wide QRS. Shape of QRS may vary.]
 - Extrasystole/ectopic beats come early – some part of the heart has depolarised prematurely
- Distinguish Ventricular Tachycardia and supraventricular tachycardia with bundle branch block:
 - Both have wide QRS
 - But Supraventricular Tachycardia has P waves (check all leads). Compare QRS with normal QRS – if similar then bundle block.
- Wolff-Parkinson-White Syndrome (a type of ventricular pre-excitation): Accessory conducting bundle, usually to LV \rightarrow short PR and QRS has abnormal slurred upstroke (delta wave)
- Treatments:
 - Atrial Fibrillation: Digoxin
 - Junctional Tachycardia: Carotid sinus pressure then adenosine
 - Atrial Flutter: Carotid sinus pressure, adenosine, flecainide, DC conversion
 - Ventricular Tachycardia: lignocaine, DC conversion
- Check **Cardiac Axis**
- Check **P wave**: shape:
 - Normal is $< 2 * 2$ small squares
 - Right atrial hypertrophy (eg tricuspid stenosis) \rightarrow peaked P
 - Left atrial hypertrophy (eg mitral stenosis) \rightarrow broad, twin-peaked P, especially in II, III, aVF
 - Potassium: $\downarrow K \rightarrow \uparrow P, \uparrow K \rightarrow \downarrow P$
- Check **conduction intervals** - PR interval:
 - From beginning of P wave to beginning of QRS = time for AP to spread from SA node to ventricular muscle.
 - Normal is 0.12 – 0.2 sec. (3 – 5 small squares)
- Description of **QRS Complex**. Width of QRS complex = time for AP to spread through ventricles:
 - Normal is ≤ 0.12 sec. (3 small squares)
 - \uparrow Height \Rightarrow \uparrow muscle mass
 - Right Ventricular Hypertrophy:
 - V1: R becomes higher (> 25 mm)
 - V6: S becomes deeper
 - Also look for:
 - Right axis deviation
 - Peaked P (right atrial hypertrophy)
 - Inverted T in V1 – V3
 - This picture is similar to a PE (which also has a Q wave in III)
 - Left Ventricular Hypertrophy:
 - V1: deep S wave
 - V6: Tall R wave (> 25 mm)
 - Inverted T wave in II, VL, V5 and V6
 - Left axis shift
 - Q waves:
 - Negative wave at start of QRS
 - If $>$ one small square wide and > 2 mm deep \Rightarrow patch of non-active muscle in the wall and the lead is ‘looking inside’ the heart, not at the wall \Rightarrow old MI. Usually permanent
 - Anterior/septal infarct \Rightarrow Q wave in V2, V3 and V4 (Left anterior descending artery)

- Anterior-lateral infarct \Rightarrow Q waves in I, II, VL. V3 – V6 (Left circumflex)
- Lateral infarct \Rightarrow Q wave in I, V5, V6
- Inferior infarct \Rightarrow Q wave in II, III and VF (\Rightarrow right coronary artery)
- Inferior-lateral \Rightarrow Q wave in II, III, aVF, V5, V6
- Bundle Branch Block
- Description of **ST segments**:
 - If raised \Rightarrow acute injury – recent MI or pericarditis. Anterior \Rightarrow V5, V6. Inferior \Rightarrow III and VF
 - Depression \Rightarrow ischaemia not infarction
- **T wave**:
 - Normally inverted in aVR and V1 (also V2 in young people and V3 in blacks)
 - If not full thickness infarct \Rightarrow T wave inversion but no Q wave (no ‘window’ into heart) \Rightarrow non-Q wave infarction
 - If abnormal QRS \Rightarrow abnormal T of no significance (repolarisation also skewed)
 - Digoxin \rightarrow T wave inversion and sloping depression of the ST segment
 - Electrolyte imbalances:
 - $\downarrow K \rightarrow$ T wave flattening
 - $\uparrow K \rightarrow$ tall, wide peaked T waves
- **QT interval**
 - $\downarrow Ca \rightarrow \uparrow QT$ interval
 - $\uparrow Ca \rightarrow \downarrow QT$ interval
- Progression following MI:
 - Elevation of ST
 - Q waves appear
 - T becomes inverted – may be permanent

ECG Abnormalities Due to Electrolyte Disturbances

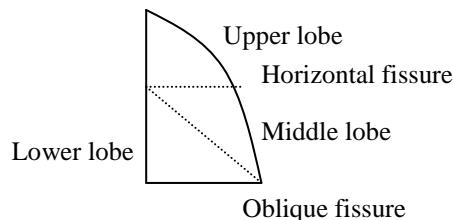
Abnormality	Common Cause	ECG	Emergency Treatment
\uparrow Potassium	Renal failure Addison's disease	Peaked T Prolonged PR Small P Wide QRS VT, VF, asystole	Calcium chloride Bicarbonate Insulin/Glucose Beta agonists Dialysis
\downarrow Potassium	Diuretics Hyperaldosteronism Vomiting Gastric aspiration	Wide, flat or inverted T Depressed ST segment Small QRS Prolonged PR Prominent U wave Large P wave	Potassium Magnesium
\uparrow Magnesium	Renal Failure	Bradycardia AV block Asystole	Calcium Chloride
\downarrow Magnesium	Alcoholism Starvation Urinary Loss Diuretics GI loss Malabsorption	Long QT Short QT Broad T VF, VT, asystole	Magnesium
\downarrow Calcium	Hypoparathyroidism Acute pancreatitis Renal failure	Long QT Elevated ST Peaked or inverted T AV block Tachyarrhythmias	Calcium Chloride

Chest X-ray

- First check:
 - Is it the right patient
 - Is it the right date
 - Is it the right way round (ie L and R)
- Then ask what is their age (and therefore likely pathologies)

- How was the film taken:
 - Normal is PA erect, inspiratory:
 - PA as all Xray sensitive tissues are on the front (breasts, eyes, gonads, thyroid) – less exposure
 - Scapula off chest (in an AP then scapula projected onto chest)
 - Differences in Supine film:
 - Air collects on front of chest not top (important for pneumothorax)
 - Fluid distributes over back of pleura not in costophrenic angles
 - Normally more blood flow in lower zones, but in supine equal vascular markings at top
 - Better venous return in supine → distended great vessels
 - To tell if it's supine where is gastric bubble: fundus = erect, body = supine
- Is the film good enough:
 - Is it rotated: medial ends of clavicle equidistant from spinous process
 - Is it a good exposure: can you see lung veins in periphery – if you can see the spine clearly then over exposed
 - Good inspiration: 5 – 7 anterior ribs on the right (hemidiaphragm is higher – must take a bigger breath to get it down) or 9 – 11 posterior ribs
- Key questions:
 - Is there any area that is lighter (\uparrow opacity)
 - Is there any area that is darker (\uparrow lucency)
 - Is there any abnormality of normally seen anatomy
- Normally seen anatomy/silhouettes:
 - Right Upper quadrant (above the right bronchi):
 - SVC: free edge abutting lung
 - Right paratracheal strip (lung abutting right side of trachea). If strip wider than 5 mm then lymph node enlargement
 - Arch of azygous in tracheal bronchial angle, just above carina. If enlarged think RH failure or IVC obstruction
 - Left Upper Quadrant (above the left bronchi):
 - Arch of aorta (aortic knuckle) and free edge of descending aorta behind heart
 - Pulmonary trunk
 - Between them is the aortic pulmonary window: should be concave, if convex then lymph node enlargement
 - Right lower quadrant (below right bronchi): Right atrium forming the border of the heart
 - Left lower quadrant (below left bronchi):
 - Border of heart = left ventricle + left auricle of atrium (NB its below the bronchi – a bulge above the bronchi must be something else)
 - Left hemidiaphragm (lower than the right)
 - Lateral view:
 - Spine should get blacker as you go down
 - Retrosternal and retrocardiac areas should be the same density
 - Left hemi-diaphragm is the one that the heart sits on
- Heart size:
 - Enlargement: greatest transverse diameter = largest horizontal distance from midline to right border + largest horizontal distance from midline to left border. If this is $> 50\%$ of greatest internal diameter then the heart is enlarged
 - Signs of left atrial enlargement:
 - 2nd heart border parallel and medial to RH border (atrium bulging around behind the RA)
 - \uparrow Density medial to this 2nd border
 - A prominent left atrial appendage
 - Elevation of the left main bronchus
 - Right atrial enlargement: bulges into right lung and elevation of right main bronchus
 - Right ventricle enlargement: Apex tilts upwards. On the lateral film, \uparrow area of contact between the heart and the sternum
 - Left ventricle enlargement: Elongates along its long axis → apex shifts down and out. Posterior bulge on the lateral film
 - Causes of global heart enlargement:
 - Sack like dilatation: due to pericardial effusion, cardiomyopathy or multi-valvular disease
 - Multi-valvular disease

- Hypertrophic cardiomyopathy
- Pericardial effusion
- Progression of pulmonary oedema:
 - ↑Prominence of upper zone vessels due to redistribution of blood to upper zones
 - Leakage → interstitial changes: peribronchial cuffing, Kerley B lines, effusion
 - Flooding of the airspaces → ‘Bats wing’ appearance
 - With treatment, resolves in the reverse order
- Ribs
 - Posterior of rib connects with midline, anterior doesn't as it turns to cartilage which isn't calcified (but maybe in old person)
 - If 1st and 2nd ribs fractured, this takes massive force, consider concurrent damage to great vessels
 - If sternum fractured, consider cardiac contusion – do cardiac enzymes
 - If 11th and 12th ribs fractured, consider damage to kidney's, liver, spleen
 - If multiple fractures: flaccid chest → Paradoxical Breathing (segment of chest moves in on inspiration)
- Lobes:



- Upper: apical, posterior, anterior
- Medial: superior, inferior
- Lower lobe: Anterior, posterior, lateral, medial, apical
- Pathology to look out for:
 - Pulmonary contusion: Opacity in parenchyma = bleeding. Should clear in 3 – 6 days (cf consolidation which may take 6 weeks to clear). May resolve leaving clots filling cavities created from shearing forces
 - Pneumothorax: must see visceral pleural edge AND no vascular markings lateral to this edge. Edge alone might be other things
 - ARDS: soft and fluffy over all the lung parenchyma
 - Aspiration: won't be symmetrical. If it's global is it the ‘bats wing’ appearance of pulmonary oedema?
 - Is it effusion or pneumonia: Pleura is 2 cells thick. If pleural cavity fills up loose sharp edge. If unsure, take another film lying on side (De Cubitus view) and see if fluid level shifts. If the opacity is heterogeneous (eg polka-dots) then pneumonia, if homogenous (a smear) then effusion
 - Miliary pattern: occurs in Tb, fungi, Thyroid cancer, *pneumoconiosis*, rarely Sarcoid
 - Cysts ⇒ cystic bronchiectasis. Especially in Cystic Fibrosis and Staph.
 - Enlarged hilum can be:
 - Enlarged vessels
 - Lymph node enlargement (like bunches of grapes): sarcoid, Tb, lymphoma
 - Cancer – usually unilateral
- Differential if CXR is normal:
 - Airflow obstruction: asthma, COPD
 - PE
 - Pneumothorax (look again...)
 - Hidden pneumonia: check apices, angles and behind both sides of the heart (can you see the diaphragm below the heart or the ribs behind the heart?)
- Chest X ray checklist:
 - A – airway – midline
 - B – bones and soft tissue. Check for gaps in bones → ?bony metastases
 - C – cardiac size and silhouette. Should be < 50% of maximal internal chest width
 - D – diaphragm – right higher than left, angles sharp, contract with lung sharp
 - E – equal volume, density symmetrical
 - F – fine detail (pleura & lung parenchyma)
 - Is upper darker than lower

- Pronounced/wider vessels in upper lobes \Rightarrow pulmonary venous congestion
- Interstitial/pulmonary oedema \rightarrow fine diffuse shadowing
- Kerley B lines \Rightarrow oedematous interlobular septa
- Fluff extending from hilum (bat's wing appearance): alveolar pulmonary oedema
- Atelectasis: dense, short, usually peripheral horizontal lines. If large then collapsed lung
- Are L & R main bronchus $<$ 75 degrees at carina
- If there are dots, are they hollow (if so then likely to be blood vessels end on)
- G – gastric bubble
- H – hilum – left higher than right, no larger than thumb + Hardware
- Don't make pathological diagnoses – say an opacity *consistent with* consolidation
- *Treat the patient not the x-ray*

Cardiovascular Risk factors*

- Ref: 1996 National Heart Foundation Clinical Guidelines for the Assessment and Management of Dyslipidaemia, NZMJ, 1996; 109:224-32
- Framework:
 - Collect information on risk factors
 - Estimate prognosis
 - Decide on Treatment based on assessment of benefits and risks:

Assessment of risk

- Absolute risk of cardiovascular disease depends on the combination of all risk factors. Treatment decisions should be based on assessment of total risk – not one factor in isolation (eg raised blood pressure or cholesterol)
- Absolute risk is usually stated as the risk of a cardiovascular event in the next 5 years (Based on the Framingham Study):
 - Very high risk: $>$ 20% risk in next 5 years. Includes by definition people with:
 - Proven cardiovascular disease (past MI, positive treadmill, stroke, claudication, etc)
 - Familiar hypercholesterolaemia and familial combined hyperlipidaemia
 - Established diabetic nephropathy (albumin excretion $>$ 300 mg/day)
 - High risk: 15 – 20% risk in next 5 years
 - Moderate risk: 10 – 15% risk in next 5 years
 - Mild risk: $<$ 10% in next 5 years
 - Over age 70, risk for all individuals is very high, and age effect dominates
- Risk factors in the Framingham tables are age, gender, blood pressure, dyslipidaemia, smoking and diabetes/IGT
- Risk factors not included in the tables are: Family history of coronary disease, physical inactivity, obesity (especially BMI $>$ 27), left ventricular hypertrophy, fibrinogen, lipoprotein (a). The presence of these should bias treatment decisions towards treatment at any level of risk.

Dyslipidaemia

- High levels of LDL ('bad' cholesterol), low levels of HDL ("good" cholesterol) : normal ratio $<$ 4.5
- LDL reflects heredity, diet (both high cholesterol & high saturated fat) and exercise
- \uparrow TAG and \downarrow HDL may be related to insulin resistance, without total Cholesterol being appreciably raised
- Raised triglyceride levels are closely related to low HDL levels \Rightarrow hard to separate their independent effects on risk
- Secondary causes: diabetes mellitus, obesity, alcohol abuse, hypothyroidism, renal disease, corticosteroids, exogenous sex hormones, pregnancy
- Levels should be measured in early adulthood, especially if other risk factors or significant family history of heart disease
- Fasting lipids best measure of TAGs (from which LDL can be inferred – more accurate than total cholesterol)
- Within 24 hours of an MI, and up to 3 months later, total cholesterol \downarrow and HDL \uparrow , so measurements over this period are not reliable
- Treatment:
 - A 10% relative reduction in total cholesterol reduces relative risk by 15 – 20% over 5 years

- Treatment goal: total cholesterol < 5 , HDL > 1, TAG < 2. TC: HDL < 4.5. Realistic goal is 25% reduction in total cholesterol through diet and drugs
- Thresholds for drug treatment following dietary treatment:
 - For very high risk: treat if TC or TC:HDL > 5.5
 - For high risk: treat if TC or TC:HDL > 6.5
 - For moderate risk: treat if TC or TC:HDL > 7.5
 - For mild risk: treat if TC or TC:HDL > 8.0
- Dietary advice: reduce saturated and trans unsaturated fats + exercise
- For drugs, see Lipid Lowering Drugs, page 53

Other Specific Risks

- Hypertension: Blood pressure > 160/95 has 5 times risk. Vibrational stress damages intima. Pressure wave tears the intima and this heals by scarring. Large pulse pressure also significant. Atheroma occurs most commonly at vascular bifurcations. See Hypertension, page 34
- Cigarette smoking: 2 times risk. Intimal microlceration (a complication to a plaque) predisposes to thrombosis. Tobacco oxidises LDL → poorly digested form that accumulates in the intima
- Diabetes: 2 times risk factor → advanced glycosylation end-products (non-enzymatically glycosylated proteins) bind to endothelium → permeable, causes cells to produce fibrous tissue

Vessel Pathology

- Arteries
 - 3 layers:
 - Intima: thin, includes endothelium, underlying thin layer of connective tissue containing smooth muscle, and elastic interna – elastic fibre layer
 - Media: thick, smooth muscle and collagen. Large arteries have elastic fibres as well
 - Adventitia: thin layer containing elastic fibres in loose connective tissue
 - 3 sizes: large (elastic), medium (muscular), small
- Veins: thin wall, large lumen, IEL intact only in large vessels, scant media, contain valves

Atherosclerosis

Epidemiology

- Causes 50% of all deaths in US – including coronary, cerebral and peripheral vascular disease
- A disease of Western civilisation. Absent in certain 3rd world ethnic groups

Aetiology

- Multifactorial
- Endothelial damage → ↑ permeability, monocyte adhesion and endothelial proliferation → intimal hyperlipidaemia with invasion of foamy macrophages → cytokines (IL1 and TNF) and growth factors (PDGF and FGF) cause inflammatory response and proliferation of smooth muscle with sclerosis; plaque thickened by organisation of superimposed thrombi

Gross Morphology

- Lesions appear in childhood as fatty streaks
- Adult plaques: discrete, yellow white random elevations, more prominent around ostia of large branches
- Plaques may have sclerotic firm surfaces or ulcerate exposing soft cholesterol laden material
- Severity increases with age

Microscopic Morphology

- Plaque: intimal lesion – deposition of cholesterol esters, necrotic debris, smooth muscle and foam cells. Chronic fibrotic inflammatory response forming a superficial fibrous cap
- Complications are ulcers with thrombi, bleeding into plaque, embolisation, calcifications, atrophy of media → aneurysms
- Reduplication of internal elastic lamina: shows with Elastin Van Geesen (EVG) stain
- Adventitial fibrosis and chronic inflammation

Complications

- Calcification → rigid pipe → ↑pulse pressure → distal atherosclerosis. (NB Calcium laid down in two ways: dystrophic calcification – Ca laid down in necrotic tissue – and metastatic calcification - ↑serum Ca → Ca laid down abnormally)
- Ulceration: fibrous cap cracks – debris discharged into lumen → embolisation/thrombosis
- Thrombosis: can embolise, or occlude artery. Cause of majority of myocardial infarcts and cases of unstable angina pectoris. If collateral circulation, can recannalise thrombosis
- Haemorrhage: a weak little new artery in the plaque bursts → pushes plaque against opposite wall

Aortic Aneurysm

Aetiology

- Severe arteriosclerosis
- 20% familial incidence → defect in connective tissue component (?type III procollagen)
- Syphilis and other bacterial infections
- Cystic medial necrosis → denudation of elastic layer
- Trauma
- Common in Marfan's syndrome (eg Abraham Lincoln). Long ulnar, femur, weak aorta, and high arched palate

Clinical

- 75% occur in abdominal aorta. Easy to repair cf thoracic and thoraco-abdominal cases
- Often asymptomatic → incidental finding
- Can cause back pain (due to retroperitoneal blood). Differential → pancreatitis
- 44% of symptomatic aneurysms rupture. ↑Distension → inevitable rupture (Law of La Place)

Pathogenesis

- Arteriosclerosis → gradual destruction of media → focal weakening of wall → ↑distensibility → ↓w + ↑r → ↑tension + ↓blood velocity ($T \propto P r/W$)
- ↑Pressure → ↑radius → ↑tension → ↑radius, etc

Gross Description

- Fusiform dilatation of severely atherosclerotic aorta with sharp superior and inferior margins
- Typically abdominal aorta, from just below ostia of renal arteries to bifurcation of aorta
- Larger aneurysms contain thick old laminated thrombus reducing patent luminal size
- Aneurysmal thrombus does not organise due to the paucity of functioning vasa vasorum in fibrotic wall

Microscopic Description

- Aneurysm wall: barely identifiable media, fibrotic lesions with focal aggregates of mononuclear cells
- Adventitia is fibrotic with chronic inflammation

Complications

- Thrombus → distal gangrene, calcification, bacterial infection (salmonella, shigella), rupture, dissection, fistula (eg aorta-vena cava)

Dissecting Aneurysms

- Usually involves the aorta
- Fatal in 75 – 90% of cases
- Causes: atherosclerosis, also hypertension, Marfan's syndrome, trauma, inflammation of media
- Pathogenesis:
 - Cystic medial necrosis: mucoid cysts in the media, elastic fragmentation and fibrosis
 - Commences as a transverse intimal tear, 90% in ascending aorta
 - Splits the media between the mid and outer 1/3
 - Proceeds down occluding branches
- Outcomes:
 - Acute perforation → sudden death
 - Subacute progression → perforation in several days
 - Chronic → rupture back into the lumen → double barrel aorta

Arteritis

- Diverse group of diseases classified by aetiology, vessel size or histologic changes

Infectious arteritis

- Wide range of organisms, pyogenic, TB, parasites, viruses, fungi, syphilis
- Vessel infected by septic emboli (\rightarrow lodges and forms mycotic aneurysm) or direct extension from adjacent abscesses
- Histology: oedema, fibrin, dense neutrophilic infiltrate
- Outcome: scarring, obliteration of lumen \rightarrow distal infarction
- Syphilis: occludes vasa vasorum \rightarrow ischaemic damage to artery, small vessel occlusion \rightarrow obliterative end arteritis, perivascular lymphocyte and plasma cell cuffing. Famous for causing proximal aortic aneurysms

Physical/Chemical Agents

- Irradiation, trauma, vascular toxins, sulphonamides, penicillin

Arteritis syndromes

- See Vasculitis, page 282

Other Vessel Abnormalities

- Arteriosclerosis:
 - = Thickening and loss of elasticity of arterial walls. Seen in chronic hypertension, and to a lesser degree with ageing
 - Hyaline arteriosclerosis: blood vessel takes on glassy 'hyaline' appearance. Reflects mild or 'benign' hypertension. Particularly seen in kidneys
 - Hyperplastic arteriosclerosis: concentric rings of increased connective tissue and smooth muscle give arteries an onion skin appearance. Signifies acceleration/malignancy of the hypertension
- Fibromuscular dysplasia: non-inflammatory thickening of large and medium sized muscular arteries causing stenosis. Most significant in renal arteries \rightarrow secondary hypertension
- Thrombophlebitis: inflammation and secondary thrombosis of veins, usually small veins as part of a local reaction to bacterial infection
- Varicose veins: enlarged, dilated, tortuous blood veins and incompetent venous valves – mainly in legs. Predisposing factors include older age, female, heredity, posture and obesity. Varicose veins at other sites include haemorrhoids (rectal), oesophageal varices and varicocoele (scrotum)
- Vasculitis: inflammation and necrosis of blood vessels – including arteries, veins and capillaries. May be due to infection, trauma, radiation, toxins or immune (eg disposition of immune complexes)
- Leukocytoclastic vasculitis: a form of hypersensitivity angiitis in the skin presenting as purpura

Ischaemic Heart Disease

- Most common cause of death in Western countries
- Incidence peaked in NZ in 1968 at 320 deaths /100,000. Now 200/100,000
- In NZ, 4,500 acute MI per year, 3,200 CIHD per year (=25% of all deaths)
- Risks factors:
 - Cigarette smoking 5.2 x
 - Hypertension 3.3 x
 - Hyperlipidaemia 3.7 x
 - Diabetes mellitus
 - Male gender
 - Family history
- Pathogenesis
 - Myocardial blood flow < metabolic demand of myocardium
 - Coronary perfusion related to:
 - Atherosclerosis occluding coronary arteries (fixed coronary stenosis), acute plaque changes (eg rupture), thrombosis, vasoconstriction
 - Differential between ostia (aortic diastolic pressure) and coronary sinus (right atrial pressure)
 - Compression of intramuscular arteries during contraction \rightarrow myocardium perfused in diastole
 - Decreased coronary blood flow also due to ↑intraventricular pressure & myocardial contraction, aortic valve stenosis/regurgitation, ↑right atrial pressure

- Cross sectional area of major vessels must be reduced by 75% to significantly affect perfusion

Hypertension

- See Measuring Blood Pressure, page 19, for measurement
- Is a risk factor not a disease
- Definition:
 - No dividing line between normal and high blood pressure. There are arbitrary levels set based on the risk of complications (the main ones being stroke, MI, heart failure and renal failure)
 - In determining whether the blood pressure is 'bad', take into account the systolic and diastolic pressure, age, sex, other diseases (eg DM, hyperlipidaemia), smoking. Older age is the greatest risk factor: treat high blood pressure in an older person regardless of other risk factors
- WHO definitions:

Category		Systolic	Diastolic
Normal		< 130	< 85
High Normal		130 - 139	85 - 90
Hypertension	Stage 1 (mild)	140 - 159	90 - 99
	Stage 2 (moderate)	160 - 179	100 - 109
	Stage 3 (severe)	180 - 209	110 - 119
	Stage 4 (very severe)	> 210	> 120

- Also classified according to retinopathy, see Hypertensive Retinopathy, page 146
- Classified as:
 - Primary/essential (what most people have – but a diagnosis of exclusion): contributing factors include hereditary, obesity, alcohol intake, salt intake (60% of patients respond to ↓salt intake – but compliance difficult)
 - Secondary causes: renal disease (eg renal artery stenosis, diabetic kidney disease, etc), endocrine (eg ↑cortisol, ↑aldosterone, acromegaly, oral contraceptives), neurogenic (eg psychogenic), sleep apnoea (major changes in baroreceptor reflexes)
- Epidemiology:
 - Prevalence ↑ with age. Older people at greater risk at any given blood pressure compared with young
 - Strong risk factor for stroke, congestive heart failure, coronary artery disease and renal failure
 - Probably 10 – 20% of older adults require treatment (ie have essential hypertension with diastolic pressure > 95 mmHg)
 - Treatment reduces related complications. Stroke risk reduces in line with BP, MI risk doesn't reduce as much for a given drop in BP
- History:
 - How accurate is the diagnosis?
 - Usually symptomless
 - *Possibly* related symptoms: palpitation, flushing, headache
 - Related risk factors: history of renal, cardiac or neurological disease
 - Asthma, diabetes, gout, renal disease: complications with drug treatment
 - Occupational
 - Diet: salt, fat
 - Smoking and alcohol
 - Family History
- Detection and assessment:
 - Blood pressure more labile in older adults ⇒ measure 2 to 3 times (in same arm). Measure standing and sitting
 - In primary hypertension usually ↑ on standing. In secondary hypertension, usually ↓ on standing
 - Basic workup:
 - Urine for protein, blood and glucose → DM, renal disease
 - FBC for polycythaemia, renal disease, alcohol
 - Electrolytes (especially K): exclude odd endocrine causes
 - ECG: any end organ damage
 - Additional tests if indicated:
 - Microscopic analysis of urine (for casts)
 - Plasma lipids
 - Blood glucose: need to modify drug treatment

- Serum Ca, PO₄, uric acid (gout – associated with hypertension, may also ↑ due to drugs)
- Echocardiogram or CXR
- Special tests for secondary causes if indicated: eg renal imaging, 24 hour urine for catecholamine metabolites (phaeochromocytoma)
- Pathology:
 - Pathophysiology: poorly understood. Older people have ↓renin, and are more responsive to Na depletion. ‘Hardening’ of arteries →↑systolic pressure. ↓Responsiveness to β-mediated vascular relaxation
 - Leads to hypertensive heart disease: left ventricular hypertrophy → relative myocardial ischaemia. Aortic valvular disease also → LV hypertrophy
 - Malignant hypertension (accelerated hypertension): hypertension leading to rapidly progressive vascular compromise. Blood vessels show fibrinoid necrosis or concentric hyperplasia (‘onion skin’ changes)

Non-drug treatment

- Remove/substitute drugs: eg NSAIDs, OCP, Prednisone
- Always attempt lifestyle changes first:
 - Stop smoking (little effect on BP, but biggest impact on risk factors)
 - Weight loss
 - ↓Alcohol (max 2 drinks per day)
 - ↓Salt intake (max 70 mmol/day)
 - ↑exercise
 - ↓Saturated fats

Drug Treatment

- When to treat:
 - Given it is such a strong risk factor, consider hypertension above systolic 140 mmHg
 - Always treat > 170 systolic or > 110 diastolic
 - Hardly ever treat < 140 and < 90 diastolic
 - In between, controversial. Consider other risks. If over 65 no other risk factors needed (eg diabetes, etc). Give considerable attention to non-pharmacological approaches for 3 – 6 months. Long term follow up necessary
 - Treat 72 older adults for 5 years to prevent 1 death, treat 43 for 5 years to prevent one cerebrovascular event
 - Aim of treatment: diastolic < 90
- Rules of thumb:
 - Use low doses of several agents, rather than increasing doses of one drug (especially thiazides)
 - First line: thiazides (with or without a potassium sparing agent) and/or β-blocker (atenolol most used in trials). If tolerate them both then add them together
 - ACE inhibitors: not so effective but rated best quality of life
 - Don’t take diuretic, ACE inhibitor and NSAIDS together (renal side effects)
 - Introduce slowly, monitor for symptoms and postural hypotension
 - Aim for 140/90, and then attempt back titration 3 monthly
- Individualise depending on co-morbid conditions:

Condition	Implication
Atrial Fibrillation	Some Ca channel blockers and β-blockers may help. Watch for drug interactions with digoxin
COPD	Avoid β-blockers (also in Asthma)
CHF	ACE inhibitors improve the CHF. If diastolic dysfunction is prominent then β-blockers or Ca antagonists
Diabetes Mellitus	ACE inhibitors delay renal failure. Thiazides worsen diabetic control. β-blockers may mask hypoglycaemic symptoms
Gout	Thiazides may worsen hyperuricaemia
Ischaemic Heart Disease	Consider β-blockers
Renal Failure	↑half life of some drugs (eg atenolol)

Voiding Dysfunction	In men with ↓urine flow, consider α-blockers (eg terazosin)
History of IHD, stroke or	Aspirin
DM	

- See Cardiovascular Pharmacology, page 51

Angina Pectoris

- Symptom complex characterised by attacks of chest pain, causing ischaemia but not infarction
- Patterns:
 - Stable angina (typical): pain on exertion, relieved by rest or vasodilators. Subendocardial ischaemia with ST-segment depression
 - Variant or Prinzmetal's angina: classically occurs at rest. Caused by reversible spasm in normal to severely atherosclerotic coronary arteries. Can see ST-segment elevation or depression
 - Unstable angina: variable, prolonged pain, pain at rest or worsening of pain in stable angina. ST-segment depression – but may be elevated. Most common complication: arrhythmias (especially VF). Within 3 months 4% will have sudden death and 15% a myocardial infarct
 - Sudden cardiac death. Usually within an hour of a cardiac event or without symptoms. Usually high-grade stenosis. Usually associated with arrhythmias, especially ventricular ectopic beats and subsequent VF
- Treatment options for stable angina:
 - Nitrates: short & long acting
 - β-blockers (↓myocardial O₂ consumption)
 - Ca antagonists
 - Aspirin
- Unstable angina:
 - = Acute Coronary Syndrome (ACS) = acute heart problems without ST *elevation*
 - Investigations:
 - ECG. Serial or continuous if high risk
 - Bloods: Troponin (repeat after 6 hours), FBC, Cr, electrolytes, CK, blood glucose. Want to test lipids/cholesterol – but false positives following an acute coronary event. Do later.
 - CXR: cardiomegaly? Pulmonary oedema? Dissection?
 - Medical therapy:
 - Aspirin: reduces progression to MI. Neither Warfarin nor Heparin confers little further benefit. Use heparin if high risk.
 - β-blockers: reduce progression to MI
 - iv nitroglycerine for symptomatic relief
 - Maybe calcium channel blockers that reduce the heart rate
 - Low risk:
 - Normal ECG and no detectable troponin despite ↑angina frequency or severity
 - Management: discharge for outpatient assessment
 - High risk:
 - If even a minor degree of ST depression or a significant elevation of troponin → minor myocardial damage so now is the time to act
 - Overlap between High Risk ACS and non-STEMI (non-ST elevation MI)
 - Management: Admit for coronary angiography and, if positive, early percutaneous coronary intervention (ie more aggressive treatment than previously)
- Long term management:
 - ↓Obesity, diabetes, smoking, ↑exercise
 - Referral to a cardiac rehabilitation programme
 - Statins if serum cholesterol raised
 - ACE inhibitors if hypertension or diabetes

Myocardial Infarction (MI)

Definition and Classification

- Old WHO definition: two out of three of: chest discomfort for > 30 minutes, enzyme rise and typical pattern of ECG involving the development of Q waves (ie normal ECG does not rule out infarction)

- New definition: Blood levels of sensitive and specific markers are raised in the clinical setting of acute ischaemia (ie ↑importance of biochemical tests). See Laboratory Diagnosis, page 38
- 2 classifications:
 - ST elevation MI versus none (ie STEMI and non-STEMI). Often ST elevation progresses to Q wave
 - Q wave versus none (older classification) ⇒ transmural or not

Epidemiology

- Same risk factors as for atherosclerosis
- 5% occur under age 40, 45% over age 65
- Oestrogen protective in women pre-menopause
- 30% mortality with 20% dying before admission

Symptoms

- Crushing chest pain (absent in 15% of cases). But < 25% with chest pain have an MI
- Can also present as epigastric, arm, wrist, or jaw discomfort with exertion or at rest
- May be associated with dyspnoea, sweating, nausea, vomiting, weakness, dizziness, fainting

Pathogenesis

- Irreversible damage in 20 – 40 minutes
- Occlusive intracoronary thrombus, overlying ulcerated or stenotic plaque:
 - Causes 90% of transmural acute MIs.
 - For blood to clot need: abnormal flow, damage to vessel wall and clotting factors.
 - Thrombus formation: activated platelets adhere to exposed collagen of damaged endothelium → release thromboxane A2 → expanding platelet mass + coagulation
- Vasospasm: with or without atherosclerosis. Postulate where no findings at post-mortem (10%) – but many of these will be thrombi that have lysed
- Emboli: from left sided mural thrombosis, vegetative endocarditis
- Arteritis: polyarteritis nodosa, Kawasaki disease
- Other: dissecting aneurysm occluding coronary ostia, ↓O₂ supply (anaemia, CO, cyanide), ↑O₂ demand (hyperthyroidism, fever)

Gross Morphology

- Transmural infarct: entire thickness of wall from endocardium to epicardium. Usually Anterior wall (50%) or posterior free wall/septum in 15 – 30%. Q wave
- Subendocardial infarct: multifocal necrosis confined to inner 1/3 to 1/2 of left ventricle wall. More commonly associated with temporary hypoperfusion (eg shock). No Q wave
- Occlusion:
 - LAD: 40 – 50%
 - RCA: 30 – 40%
 - LCA: 15 – 20%
- Gross changes over time:

18 – 24 hours	Pallor of myocardium – anaemic, grey brown (cf normal brown-red)
24 – 72 hours	Pallor (yellow/brown) with increasingly defined hyperaemia border
3 – 7 days	Hyperaemic border (darker brick red) with central yellowing, haemorrhagic areas
10 – 21 days	Maximally yellow and soft with vascular margins (red edge – granulation tissues moves in)
7 weeks	White fibrosis

Microscopic Appearance

- | | |
|--------------|---|
| 1 – 3 hours | Wavy myocardial fibres |
| 2 – 3 hours | Staining defect with tetrazolium |
| 4 – 12 hours | Coagulative necrosis with loss of cross striations, oedema, haemorrhage, early neutrophil infiltrate (WBCs with multilobed nuclei), loss of myocardial striations |

18 – 24 hours	Continuing coagulation necrosis, pyknosis (margination) of nuclei (healthy myocardial nuclei are usually central)
24 – 72 hours	Total loss of nuclei and striations, heavy neutrophilic infiltrate
3 – 7 days	Macrophage and mononuclear infiltration, fibrovascular response begins (starts at edges), myocardium at its weakest
10 – 21 days	Prominent granulation tissue: fibroblasts and neovascularisation, macrophages (tissue scavengers – high fat content → yellow, high iron → brown), plasma cells
7 weeks	Fibrosis

Laboratory Diagnosis

- Troponins:
 - Increases highly specific for MI injury – but not synonymous with MI or ischaemia, but probably indicates irreversible injury
 - Increases above the 99th percentile are significant (lower than previously)
 - Prognosis related to degree of elevation
 - Rises no faster than CK (ie starts to rise within 3 – 12 hours) and more expensive but substantial rise after MI (400 fold)
 - Causes besides MI:
 - Subendocardial injury from wall stress in left ventricular hypertrophy (eg heart failure)
 - Right ventricular injury in severe PE
 - Direct trauma (eg contusion)
 - Toxic injury by drugs or in septic shock
 - Myocarditis
 - Cardioversion
 - Troponin T
 - = Cardiac troponin T, cTnT, TnT: only available from Boehringer Mannheim
 - Normal < 0.03 µg/l
 - Increases in renal failure due to ↓clearance (⇒ false positive)
 - Troponin I:
 - Everyone else's test. Normal value depends on which assay is used
 - I remains elevated for 5 – 9 days and T for 2 weeks. Better marker for recent MI than LDH. Harder to interpret in re-infarct – don't know whether it's the 1st or 2nd infarct
 - Test on admission to either see if already raised (poor prognosis) or to establish baseline
- CK – total: not specific to myocardial injury. Do baseline and use to check for reinfarction (Troponins not so good for this)
- Older tests:
 - CK – MB fraction:
 - MM fraction is in both skeletal and myocardial muscle. But 15 – 40% of cardiac CK is MB, compared with 2% skeletal. BB found in brain, bowel and bladder. The MB fraction is therefore very specific
 - MB fraction rises within 2 – 8 hours. Dissipates within 1 – 3 days. So also a good marker of reinfarction
 - CK – MB isoforms: Ratio of isoform 2 to isoform 1 > 1.5 ⇒ early acute MI (changes before CK- MB elevated). Requires electrophoresis, so labour intensive. False positives with heart failure
 - Myoglobin: Oxygen binding protein in skeletal and cardiac muscle. Elevated before CK-MB, but is not specific to cardiac muscle. Negative myoglobin can help rule out MI
 - LDH: supplanted by other tests. Rises later (24 – 48 hours) and elevated for 7 – 14 days. Isoenzyme measurement of LDH 1 and 2 necessary for cardiac specificity
 - AST and ALT: intermediate timing but rather non-specific
- Other Investigations: CXR, echo, ABG, FBC, ?perfusion scan, ?amylase

Management*

- Exclude differentials:
 - Aortic dissection
 - Pericarditis
 - PE or other causes of pleuritic chest pain

- Peptic ulcer
- Investigations as for Unstable Angina, see page 36
- They will be frightened. Reassure. > 90% survival if low risk (< 60, no diabetes, no past history, pulse < 100)
- High flow O₂ (unless CO₂ retaining)
- Morphine 5 – 15 mg iv at < 1 mg/min (+ antiemetic eg metoclopramide 5 – 10 mg iv). Effects: analgesic, anxiolytic, anti-arrhythmic, venodilatory
- Restoring/Maintaining vessel patency:
 - Aspirin 300 mg (unless contra-indicated)
 - Thrombolysis:
 - Indicated if with 12 hours of MI
 - Best within 60 mins
 - Contraindications:
 - General bleeding tendency: warfarin, haemophilia, severe liver disease, thrombocytopenia
 - Local bleeding risk: Past haemorrhagic stroke or recent surgery, prolonged resuscitation (→ rib fractures, contusion, etc), peptic ulcer, GI bleeding, pregnancy, cavitating Tb
 - Severe hypertension (systolic > 200, diastolic > 120)
 - Pre-existing thrombosis that might embolise (eg endocarditis, aortic aneurysm)
 - Options:
 - Streptokinase: restores perfusion in 30%
 - TPA: restores perfusion in 54%. Expensive. Use tPA if previous reaction to SK, or if SK has been used between 1 year and 5 days ago
 - Complications: 1% risk of stroke
 - Watch this space for platelet receptor blocking drugs (eg IIb/IIIa inhibitors)
 - Consider for primary angioplasty (acute stenting of an occluded coronary artery) if large anterior infarct refractory to thrombolysis
- Management of preload, afterload and heart rate and rhythm:
 - Glyceryl trinitrate
 - ACE inhibitor + β-blocker (unless contra-indicated)
 - Bed rest
- Monitor ECG, BP, cardiac enzymes, ABGs
- Stop smoking
- Early stress/treadmill test

Prognosis

- Good prognostic indicators:
 - No pre-existing hypertension
 - Normal heart size
 - No post MI pulmonary oedema
 - No significant arrhythmias after day 1
 - No post-MI angina
- If good prognosis, discharge on aspirin and β-blocker. Add an ACE inhibitor if ↓LVF. Consider a statin if ↑lipids.

Complications

- 35% die within one year, 10% per year thereafter. NZ overall hospital mortality 19%
- Arrhythmias and conduction defects: eg premature ventricular beats, sinus bradycardia, VT, VF, heart block
- Extension of infarction, re-infarction
- Congestive heart failure (pulmonary oedema): everyone who's had a significant MI will have some degree of this
- Cardiogenic shock: if more than 40% of the left ventricle is infarcted. 70 – 90% die
- Pericarditis: fibrinous adhesions in the pericardium overlying the infarct (Dressler's syndrome – autoimmune adherent pericarditis – occurring 2 – 6 weeks post MI or cardiac surgery. Treatment – steroids)
- Mural thrombosis → embolisation
- Myocardial rupture → tamponade. Maximum incidence day 5 - 7. Can include rupture of interventricular septum
- Papillary muscle rupture or infarct → mitral incompetence

- Ventricular aneurysm formation: 12 – 20% of cases
- Ischaemic cardiomyopathy: severe atherosclerosis involving all major branches → inadequate vascular supply → myocyte loss and interstitial fibrosis → ↓compliance & dilation → compensation by myocyte hypertrophy → slow progressive heart failure and enormous heart size (up to 2 to 3 times normal)
- Time to complications:
 - 1 – 3 days: arrhythmia, CHF, pericarditis
 - 5 – 7 days: rupture
 - Later: recurrent MI, angina, embolism from mural thrombosis, mitral regurgitation, Dressler's syndrome (Post MI syndrome)

Arrhythmias

- For cardiac arrest rhythms (VT, VF, Torsade and asystole) see Cardiac Arrest Rhythms, page 479

Atrial Fibrillation

- = a type of supra-ventricular arrhythmia
- Mechanism:
 - Wave of depolarisation circulates in atria at much faster rate than the discharge from the SA node. Disorders changing the conduction characteristics of the AV node predispose to AF: ↑atrial size, fibrosis, inflammation, thyrotoxicosis, ischaemia, altered autonomic tone, alcohol use, after bypass surgery (30%), after valve replacement surgery (50%)
 - AV node receives irregular impulses at a rate of 250 – 400 per minute. Conducted through the node at a frequency dependent on the pathway's refractory period
 - Typical ventricular rate is 120 per minute: but this may ↑ if sympathetic stimulation (→ ↓refractory period) or alternative conducting path to the AV node (eg Wolf-Parkinson-White syndrome)
- Epidemiology: most common cardiac arrhythmia. M > F. 5% of over 70s
- Causes:
 - IHD: especially post MI
 - Mitral valve disease
 - Alcohol
 - Thyroid disease
 - Idiopathic
- Potential implications:
 - Thrombo-embolism: Especially cerebral (also mesenteric arteries or lower limbs). If no other risk factors then 1% per year. 5% if one other risk factor (age over 65, ↑BP, heart failure, diabetes, IHD, previous embolism, RF). If RF and AF then 20% annual rate
 - Reduced cardiac output: ↓Ventricular filling → ↓Cardiac output → heart failure or ↓exercise tolerance. Also high ventricular rate → ↓filling → ↓CO
 - Other symptoms: palpitations (25%) and dizziness or syncope (20%)
- Diagnosis: *should always be confirmed by ECG*. Ventricular rhythm in AF can be deceptively regular, and not all irregular rhythms are AF (eg variable AV block, ventricular or atrial ectopics)
- Assessment:
 - Exclude thyrotoxicosis
 - Manage contributing MI, respiratory disease or alcohol abuse
 - Check electrolytes
 - Assess cardiovascular risk factors: eg glucose, lipids
 - Echocardiogram to assess atrial size or abnormal ventricles (eg valvular heart disease). These are harder to cardiovert (also have a higher risk of embolism). Echocardiogram is poor at detecting thrombi (trans-oesophageal echocardiogram is better)
- Management:
 - Cardioversion: indicated if onset is within 24 – 48 hours and no other risk factors (eg no atrial enlargement or ventricular abnormality). Involves general anaesthetic and synchronised DC shock at 100 then 200J. Successful in about 85%. May need anticoagulation for cardioversion (thrombi may get dislodged if normal rhythm returns).
 - Chemical cardioversion: flecainide and amiodarone – successful in 60 – 90%. (Digoxin does *not* cardiovert)
 - > 50% revert in one year if no ongoing drug treatment

- Drug treatment: consider digoxin (increases heart block → slows ventricle → improved pump action), flecainide (in those without structural heart disease), Amiodarone (extensive toxicity issues) or Sotalol:

Agent	Action	Adverse effects
Amiodarone	Prolongs action potential, β -blocker activity. Hepatic metabolism, active metabolites. $T_{1/2}$ of weeks.	Pulmonary fibrosis, thyroid and hepatic dysfunction (do baseline bloods), muscle weakness, peripheral neuropathy, skin discolouration
Digoxin	\uparrow vagal tone, renal elimination, $T_{1/2} = 36$ hours	Nausea, vomiting and confusion. $\downarrow K$ (eg diuretics) $\rightarrow \uparrow$ toxicity. Diltiazem, amiodarone and flecainide $\rightarrow \uparrow$ digoxin concentration.
Diltiazem	Ca channel blocker. Hepatic elimination. $T_{1/2} = 4$ hours.	Hypotension, headache, bradycardia, oedema, heart failure. \uparrow Digoxin levels.
Flecainide	Na Channel blocker. Renal and hepatic metabolism. $T_{1/2} = 10 - 17$ hours	Sudden cardiac death in those with structural heart disease, CHF or heart block
Metoprolol	β -blocker. Hepatic metabolism. $T_{1/2} = 4$ hours. High first pass metabolism	Hypotension, heart block, worsening of heart failure if larger doses, asthma
Sotalol	β -blocker, prolongs action potential. Renal elimination. $T_{1/2} = 8$ hours	Ventricular arrhythmia, hypotension, heart block, worsening of heart failure, asthma

- Antithrombotic therapy: Reduces annual risk in those at risk from 5% to 1.5% (60% relative risk reduction), with 1% having material anti-coagulant side effects. Use warfarin with a goal of an INR from 2 to 3. Use aspirin if warfarin contra-indicated (only 10 – 15% relative risk reduction)
- Atrial flutter: probably due to atrial re-entry. Regular atrial saw tooth pattern with ventricular beat every 3:1 or 4:1. If unstable hypotension, synchronised counter-shock at 50J (treat as for AF)

Sinus Arrhythmia

- Normal sinus rhythm: rate 60 to 100 per minute, P wave upright in leads I, II and AVF
- Sinus tachycardia:
 - \uparrow discharge of sinus node. Rate is > 100 /minute and regular
 - P wave is upright in leads I, II, AVF. Treat underlying cause
- Sinus bradycardia:
 - Constant and normal PR interval
 - < 60 bpm: but this is relative. An athlete may normal at 40, and a hypovolaemic patient bradycardic at 65 bpm
 - Causes: SA node disease, \uparrow parasympathetic tone, drug effect
 - Treat if hypotension or ventricular escape beats present
 - Treatment: atropine (0.6 mg) unless MI, transthoracic pacing, dopamine or adrenaline
- Sick Sinus Syndrome: Common in elderly. Bradycardia +/- arrest, AV block, or SVT alternating with bradycardia/asystole (Tachy-Brady Syndrome). Pace if symptomatic

Other Abnormal Rhythms

- Atrial tachycardia (paroxysmal atrial tachycardia) – SVT (Supraventricular Tachycardia):
 - Narrow QRS complex (always exclude atrial flutter with 2:1 block)
 - Often abrupt onset, last for seconds to many hours, then abrupt offset
 - Rate is usually 160 – 200/min
 - Therapy: vagal stimulation (carotid massage, one side at a time), adenosine, amiodarone, beta-blockers or digoxin. If LV failure, chest pain or HR > 220 bpm then synchronised counter-shock
- Premature Atrial Complexes (PAC): atrial ectopic beats. Small spike before premature but normal width QRS
- Junctional or Nodal rhythm: regular rhythm. May be no detectable P wave (due to retrograde firing into atrium) or inverted P-wave with short PR interval. P wave may be buried in QRS complex. Rate of 40 – 60 bpm. Reduction in atrial filling. Treatment often not indicated

- Premature Ventricular Complexes (PVC's): bizarre, wide QRS complexes triggered by an ectopic ventricular focus. Most common post-MI rhythm. Unifocal PVC's (each complex looks the same) or multifocal (each complex looks different from others)

Heart Block

- Atrioventricular block/Heart Block: Delay or interruption in conduction between atrium and ventricle
 - First degree (partial block): PR interval prolonged beyond 0.2 secs (5 small squares). Often seen in normal people. ?Acute MI or Rheumatic Fever. No urgent action needed.
 - Second degree AV block (partial block): some impulses are conducted and some not. \Rightarrow Heart disease. Often seen in acute MI:
 - Mobitz type 1 (Wenckebach): progressive prolongation of PR interval before an impulse is completely blocked – then sequence starts over. Usually transient and prognosis is good
 - Mobitz type 2: PR interval does not lengthen but some beats are not conducted. May lead to bundle branch block (\rightarrow wide QRS), transvenous pacing may be required
 - 2:1 block (every second beat gets through). Also 3:1 block. May need pacing if ventricular rate too slow.
 - Third degree (complete heart block): no conduction – either at AV, bundle of His or bundle branch level. More often fibrosis than ischaemia:
 - At level of AV node: junctional escape pacemaker will fire at 40 – 60 bpm with normal QRS. Prognosis favourable. Due to \uparrow parasympathetic tone from inferior MI or drug effect
 - At infranodal level: Implies extensive disease of both bundles. Associated with anterior MI. Distal escape rhythm, slow rate (<40) plus wide QRS, possibly asystole. Management: transvenous or transthoracic pacing, dopamine or adrenaline, pacemaker

Drugs for Acute, Life Threatening Arrhythmias

- For tachycardias:
 - Ventricular Tachycardia:
 - Lignocaine: dose 1 – 1.5 mg/kg by slow iv bolus, followed by infusion of 1 – 4 mg/min. Reduce dose in heart failure, shock, > 70 years, β blockade & hepatic disease. Side effects include convulsions. Action on sodium channels reduces myocardial excitability, especially in ischaemic myocardium. Raises threshold for VF, and **suppresses VT and ventricular ectopy**. Should be considered in VF after 3 defibrillatory loops. No evidence of usefulness in converting VF but may prevent return to VF. Reduces blood pressure and slows the heart rate
 - Bretyllium: anti-adrenergic, although initially causes adrenergic stimulation (for 20 minutes), raises VF threshold. Use if lignocaine fails
 - Procainamide: powerful antiarrhythmic and strong negative inotropic agent, but slow to act. Use where lignocaine has failed to suppress recurrent ventricular tachycardia
 - Magnesium: prevention and treatment of refractory ventricular arrhythmias
 - SVTs:
 - Adenosine: slows sinus rate and AV conduction. Use for **SVT due to re-entry**. Very short $T\frac{1}{2}$
 - Verapamil: Ca blocker. Suppresses pacemaker activity in SA and AV nodes. For SVT where adenosine has failed
 - Amiodarone: delays repolarisation with less cardiac depression than other antiarrhythmics. Good for SVT, less so for ventricular arrhythmias. Via central line, long $T\frac{1}{2}$
 - β -blockers: useful in treatment of hypertension, supraventricular arrhythmias and recurrent VT where LV function is not severely impaired. E.g. propranolol (unselective), atenolol ($\beta 1$ selective), metoprolol (relatively β selective), labetalol (α & β selective, short acting, for acute hypertensive crises), sotalol (non-selective β blocker + antiarrhythmic), esmolol (ultra-short acting β block)
- For bradycardias:
 - Atropine: Competitive anticholinergic at muscarinic nerve endings. Enhances SA discharge and AV conduction. Use in **bradycardia or AV block**. Care in MI – may increase pulse \rightarrow extension of ischaemia
 - Isoprenaline: β agonist - use for significant bradycardia refractory to atropine. Use dopamine or adrenaline first
- Other supra-ventricular arrhythmias:
 - Digoxin: \uparrow force of contraction and \downarrow AV conduction – for heart failure and supraventricular arrhythmias (particular AF). Avoid in recent MI, heart block, renal impairment, and hypokalaemia

- Dopamine: for treatment **complete heart block**. A catecholamine. Infuse at 5 – 20 µg/kg/min. Adjust to keep heart rate at 60 beats per minute. ↑renal blood flow (\rightarrow ↑renal output) through renal vasodilator and due to ↑CO and perfusion generally
- Others:
 - Inotropes: dopamine and dobutamine – for supporting blood pressure once cardiac output has been established. Useful in cardiac failure secondary to ischaemia.
 - Nor-adrenaline: intense vasoconstrictor – use for restoring MAP where vasodilation induced hypotension
 - GTN: venous vasodilator - ↓blood pressure and improve artery blood flow. Preload and afterload reduced
 - Diuretics: frusemide – also causes venodilation (\rightarrow ↓preload)
 - Antihistamines: H1 antagonists (promethazine / Phenergan), H2 antagonists (ranitidine)

Emergency cardiac pacing

- Complete heart block most common indication. Also for non-response bradycardias and asystole with P waves
- Transcutaneous/transthoracic pacing: Electrodes over apex and sternum. Sedation + analgesia required. Temporary measure only
- Transvenous pacing: via arm or neck vein into right atrium or ventricle

Valvular Heart Disease

- = Stenosis, insufficiency/regurgitation or mixed
- Insufficiency may be due to diseased cusp or supporting structures (valve ring, chordae tendinae, papillary muscles, ventricular wall). Can be acute or chronic
- Stenosis: disease of valve cusps, usually always chronic
- See Heart Murmurs, page 23 for clinical descriptions

Aortic Stenosis

- Compared with regurgitation/incompetence:
 - Have different effects on the LV (can't have severe stenosis and severe regurgitation together):
 - Stenosis: ↑pressure but no ↑ in volume. LV tolerates pressure loads less well than volume loads → stenosis is the worse of the two
 - Regurgitation: ↑volume but no ↑ in pressure. However, some ↑ in afterload due to ↑stroke volume
- Causes or aortic stenosis:
 - Post inflammatory scarring (eg rheumatic fever): 10%
 - Senile (degenerative) aortic stenosis: commonest, in 8th – 9th decade
 - Calcification of deformed valve in 6th – 7th decade (associated with coarctation \Rightarrow check for radio-femoral delay)
 - Congenital stenosis
 - Infective
- Symptoms: Occur late
 - Dyspnoea and chest tightness related to exertion
 - Exertional syncope: due to inability to increase CO and transient ventricular arrhythmias
 - Angina pectoris/MI, fibrosis, ventricular arrhythmia and sudden death due to impact on myocardial O₂ supply and demand:
 - ↑↑ O₂ demand due to ↑pressure and LV mass (\uparrow LV workload \rightarrow concentric hypertrophy)
 - ↓↓coronary blood flow due to ↓diastolic aortic pressure ↑coronary vascular resistance and ↑systole compared with diastole \rightarrow ↓time for perfusion
 - → ischaemia
 - No pulmonary oedema unless eg mitral problems secondary to LV hypertrophy, etc
- Signs:
 - Sounds:
 - Harsh systolic ejection murmur (unless in severe LV failure) +/- systolic ejection click and a short aortic diastolic murmur. Heard in base, apex and carotids
 - May have paradoxic (reversed) splitting of S2 if severe stenosis or LBBB. 3rd and 4th sounds common
 - ↓Pulse pressure and low blood pressure

- Slowing and shuddering of the carotid upstroke
- LV hypertrophy on ECG or x-ray and heave on examination. Palpable LV hypertrophy with a dynamic quality is more related to incompetence – the ventricular impulse reflects stroke volume more than pressure
- LV failure: progression from LV hypertrophy to LV dilation in late stages
- AF in 10%
- Diagnosis:
 - Often a discrepancy between symptoms and severity. Pre-symptomatic progression is highly variable
 - Usually at least some regurgitation as well
 - ECG: LV hypertrophy, occasionally left or right BBB
 - Pressure differential with Doppler → estimate valve area
- Gross:
 - Look for commissural fusion (rheumatic)
 - Heaped up calcified masses in leaflets. Beginning at the base ⇒ senile, beginning at the edge ⇒ abnormal valve
- Management:
 - If mild/moderate (ie < 50 mmHg pressure gradient across the valve) then monitor
 - Fix/replace valve *before* LV failure
- Complications:
 - Sudden death
 - LVF
 - Conduction defects
 - Infective endocarditis
 - Embolisation
- Differential:
 - Can rarely be due to supraventricular or subvalvular lesions, with no problem with the valve
 - Left ventricular failure
 - Hypertrophic obstructive cardiomyopathy: pulse is jerky and upstroke rapid. Longer, harsher murmur best heard at the left sternal edge
 - Hard to confuse with mitral regurgitation (!!): Pansystolic murmur and rapid upstroke
 - Coarctation

Aortic Regurgitation

- Causes:
 - Intrinsic valvular disease:
 - Acute lesions: Rheumatic fever, *infective endocarditis* (have high index of suspicion), traumatic rupture, aortic dissection (may also have dissected coronary arteries → MI)
 - Chronic lesions: Congenital lesions, rheumatic heart disease, arteritis, aortic aneurysm, collagen diseases, ankylosing spondylitis and Reiter's Syndrome (may be secondary to aortitis)
 - Aortic disease: degenerative aortic dilatation, syphilitic aortitis, Ankylosing Spondylitis, rheumatoid arthritis, Marfan's syndrome
- Key features:
 - LV hypertrophy
 - Large aorta
 - ↑Stroke volume
 - Wide pulse pressure eg 140/50 (↑systolic due to extra work of the heart, ↓diastolic due to back flow)
- Symptoms:
 - Acute: dyspnoea – often paroxysmal, orthopnea, pink frothy sputum. Chest pain, sudden death, etc. If sub-acute, possibly embolisation
 - Chronic: Symptoms unrelated to severity. Either awareness of ↑force of contraction (palpitations) or LV disease/failure
- Signs:
 - Pulses: prominent pulsations in the neck (Corrigan's Sign), throbbing peripheral pulses, prominent apex beat over a wide area
 - Auscultation: high-pitched, blowing diastolic murmur beginning immediately after S2. The more severe the longer it lasts. Systolic flow murmur

- Pathogenesis:
 - Acute: ↑LV blood volume → ↑left atrial and pulmonary pressure → oedema. ↑Pressure inside a non-compliant pericardium → ↑RH pressures. ↓Myocardial flow due to ↓aortic diastolic pressure and constricted pericardium → ischaemia, further dysfunction, etc
 - Chronic/Gradual: → eccentric hypertrophy with low filling pressure. ↑Stroke volume → ↑systolic pressure → baroreceptor reflex → peripheral vasodilation → further widening of the pulse pressure. Copes with tachycardia better than stenosis: ↓proportion of cycle in diastole → ↓proportion of blood flowing back into the ventricle. However, ↑peripheral resistance (eg cold, iso-tonic exercise, sympathetic nervous stimulation) → ↑pressure load on the heart
- Complications:
 - LV failure + myocardial fibrosis (secondary to hypertrophy, ischaemia, etc) late in the progression
 - Infective endocarditis
 - Conduction defects less common
 - No pulmonary oedema unless LV hypertrophy
- Differential diagnosis:
 - Pulmonary regurgitation + pulmonary hypertension
 - Other causes of rapid run-off: patent ductus, arterio-venous fistula

Mitral Stenosis

- Causes: rheumatic heart disease, infection (less common than aortic) → fusion of the leaflets
- Symptoms: dyspnoea, PND, haemoptysis, arrhythmia (→ palpitations), RH signs if pulmonary hypertension
- Signs:
 - Loud S1, opening snap after S2 (loudest at apex)
 - Long, loud diastolic murmur accentuated just before S1 (atrial systole – not if AF). Loudest with bell at apex and left lateral side
 - Pulmonary oedema is worse than in other causes (eg mitral regurgitation)
 - If pulmonary hypertension then low cardiac output failure → thin patient, peripheral cyanosis, cool extremities, small pulse volume. Dilated veins and cyanosis of cheeks = mitral facies
- Leads to:
 - LA enlargement:
 - → pulmonary hypertension (> 7.5 mmHg/L/min) and pulmonary oedema
 - → AF
 - Bronchitis
- Investigations:
 - ECG: broad P wave, RV hypertrophy (NB – LV enlargement is not typical – key differential with mitral regurgitation)
 - X-ray: LA enlargement, RH enlargement
 - Echo: good at imaging the mitral valve
- Differential: Left atrial myxoma (much less common)
- Treatment:
 - Prophylaxis for RF (till 20) and infective endocarditis (eg dental work)
 - Surgery: valvotomy, balloon valvuloplasty, replacement

Mitral Regurgitation (MR)

- Causes:
 - Abnormalities of leaflets:
 - Rheumatic heart disease → post inflammatory scarring
 - Infective endocarditis
 - Degenerative change
 - Floppy valve syndrome = mitral valve prolapse. Immature haemodynamic changes (⇒ normal heart size, etc). Common - ?5-10% of young women. Mid/late systolic murmur +/- mid/late systolic click. Complications (3% of affected) are infective endocarditis, mitral regurgitation, and embolism of leaflet thrombi
 - Congenital
 - SLE can cause Libman-Sacks endocarditis: sterile immune mediated endocarditis mainly affecting underside of mitral valve (cf other vegetative endocarditis on top)
 - Abnormalities of tensor apparatus: Previous MI: e.g. fibrosis or rupture of papillary muscle

- Abnormalities of LV cavity or valve ring:
 - Calcification of mitral ring (especially elderly women)
 - LV enlargement (whole ventricle expands). Dilatation of the mitral annulus and lateral displacement of the papillary muscles
 - Hypertrophic cardiomyopathy (thickening in parts of wall – e.g. enlarged septum disrupts flow to aortic valve). Anterior displacement of the anterior leaflet
- Existing MR – begets MR. Enlargement of LV pulls posterior leaflet away from the mitral orifice
- Signs:
 - Pan-systolic murmur: regurgitation throughout the whole of systole. Loudest at apex. Radiates over precordium and into axilla. No S1. No opening snap unless concurrent stenosis. Early diastolic flow murmur
 - In severe MR, Aortic valve closes prematurely → split S2
 - S3 caused by sudden tensing of papillary muscles, chordae tendinae and valve leaflets
 - Small volume pulse
- Significant difference between acute and chronic presentations:
 - Pulmonary oedema and RV overload much more significant if acute. In chronic, enlargement of the LA reduces pulmonary ‘back flow’
 - AF better tolerated than in mitral stenosis
 - RHF rare unless acute presentation or LVF
- Leads to:
 - Eventually leads to LV and LA hypertrophy (may take decades)
 - AF common – mostly correlated with age
 - Infective endocarditis (in 20%)
 - Systemic embolisation
 - Pulmonary hypertension (but much later compared with mitral stenosis)
- Differential:
 - Hypertrophic cardiomyopathy: both long systolic murmurs, but MR radiates to the axilla, hypertrophic cardiomyopathy radiates centrally
 - VSD

Tricuspid Regurgitation

- Commonest cause is right heart failure/enlargement secondary to left ventricular failure. Left atrium is also likely to be enlarged → AF common too

Infective Endocarditis

- = Infection of mural endothelium or heart valves. May also include the proximal aorta
- See also Rheumatic Fever, page 602

Classification

- Now all called infective endocarditis
- Acute bacterial endocarditis (ABE):
 - < 6 weeks duration
 - Virulent organisms
 - Normal valves (eg IVDU)
 - Bulky friable vegetations: may extend to adjoining endocardium and chordae tendinae. Destructive (directly proportional to virulence of organism). Much more destructive than Rheumatic Fever. Microscopically vegetations show a suppurative exudate, fibrinous thrombi, and large bacterial colonies destroying valve substance
- Sub-acute bacterial endocarditis (SBE)
 - > 6 weeks duration
 - Avirulent organisms: normal flora
 - Abnormal valves
 - Evolution slower, gradual valvular dysfunction, flatter vegetations with deeper chronic inflammatory component including a vascular fibrous tissue healing response

Predisposing Factors

- 1950s: rheumatic heart disease (most cases) – affect 15 – 35 year olds
- 1990s: degenerative, rheumatic, congenital (low pressure side of a septal defect gets infected), prosthetic valves – affects 50 year olds

- Circulatory factors:
 - Regurgitant blood stream (incompetent valve)
 - Large pressure gradient across valve (i.e. rarely right heart except IVDU)

Anatomic sites of infection

- Nearly always where there's a pre-existing abnormality
- Usually on the top of the valve
- Incompetent mitral and aortic valves: 40% mitral, 40% mitral and aortic valve
- Calcific aortic stenosis
- Prosthetic heart valves
- Congenital septal or valve defects
- Also in Intra-venous drug users (IVDU) with normal hearts (Right side commonly affected).

Causal organisms

- In theory: any organism (including fungi and chlamydiae)
- In practice:
 - Native valves:
 - Streptococci: 70%
 - Staph: 20 – 25%
 - Miscellaneous (including enterococci) 5%
 - Culture negative 5%
 - Prosthetic valves:
 - < 3 months (early PVE): staphylococci > streptococci
 - > 3 months: staph = streptococci
 - Streptococcal causes of endocarditis:
 - Oral Commensals: Viridans Streps – more in younger people, good at sticking, don't cause much infection elsewhere: *S. sanguis*, *s. salivarius*, *s. mitis*, *s. milleri*, *s. mutans*
 - Faecal: called enterococcal
 - Staphylococcal causes:
 - *S. aureus*: coag +ive – 60% mortality (common in intravenous drug user)
 - *S. epidermidis* + 20 others: coag -ive – 40% mortality
 - Miscellaneous causes: *Haemophilus*, *Actinobacillus*, *Cadriobacterium/Candida Albicans* (\uparrow in prosthetic valves, mortality 100%), *Eikenella*, *Kingella*

Pathogenesis of infection

Abnormal valve →

NBTE (non-bacterial thrombotic endocarditis) – little blood clots – we all have them but \uparrow risk on a deformed valve →

Transient bacteraemia from possibly trivial infection → adherence of bacteria →

Acute inflammatory reaction – WBCs, fibrin & platelets laid down →

Mature vegetation – sheds bacteria

Diagnosis

- Always a differential in pyrexia of unknown origin. Malaise, weakness
- Existing immunosuppression, neutropenia, diabetes, and alcohol increases risk
- Heart murmur, isolated petechiae (eg nail beds, retinal) and splenomegaly significant
- Blood culture: 3 times – organism load in blood may be low
- Echocardiogram (although may miss flat vegetations)

Complications

- Valvular insufficiency or stenosis (aortic stenosis → LV hypertrophy → coronary artery insufficiency)
- Local extension: down septum, into wall of aorta, perforated valve, suppurative pericarditis, ring abscesses
- Embolism: small infarcts (e.g. in kidney cortex) or abscess (each emboli has bacteria in it) eg in lungs
- Mycotic aneurysms, focal and diffuse glomerulonephritis
- Septicaemia
- Antigenaemia: antigen/antibody complexes → skin lesions, clogged up kidneys

Treatment

- Identify causal organism with antibody sensitive tests (MIC & MBC)
- Empiric antibiotic therapy - regimes:
 - Staphylococcal: Flucloxacillin (or vancomycin) 2g iv 4 hourly for 2 weeks, then 1 g orally 6 hourly for 4 weeks
 - Streptococcal: penicillin + gentamycin or amoxycillin + gentamycin iv for 2 weeks, then 4 weeks oral

Heart Failure

Background

- = Pump function is inadequate to maintain body homeostasis → Na and H₂O retention
- ↑ Left atrial pressure above 25 mmHg → transudate of ECF into alveoli → pulmonary oedema
- 20% have infarcts without knowing it
- Strong association with old age. A common diagnosis amongst the most disabled elderly
- Symptoms may be non-specific: ↓energy, nausea, poor appetite, poor mobility, confusion, ↓sleep etc

Classification

- Classify as:
 - High output failure: due to ↑O₂ requirements and heart can't keep up. Happens quicker if pre-existing heart disease. Eg anaemia, pregnancy, hyperthyroidism, Paget's disease. Initial features of RH failure. Progresses to LH failure
 - Low output failure: Inadequate output (ejection fraction < 0.35 – 0.40) or only adequate with high filling pressure:
 - Excessive preload: eg mitral regurgitation or fluid overload
 - Pump failure due to heart muscle disease, restricted filling, inadequate heart rate (eg heart block, post MI)
 - Chronic excessive afterload (eg aortic stenosis, hypertension)
- Can also classify as diastolic dysfunction (eg poor filling due to, for example, tamponade or restrictive cardiomyopathy) or systolic dysfunction (eg poor contraction due to a large floppy heart)
- **Left HF** → pulmonary oedema:
 - Caused by:
 - Ischaemic heart disease
 - Hypertension
 - Aortic and mitral valve disease (aortic stenosis/rheumatic heart disease)
 - Myocardial disease
 - Hypertrophied L ventricle → secondary atrial enlargement → atrial fibrillation
 - Leads to:
 - ↓Renal flow →Na retention → oedema
 - Pulmonary hypertension → pulmonary oedema and bronchospasm
 - Symptoms: exertional dyspnoea, orthopnoea, PND, wheeze ('cardiac asthma'), cough + pink froth, haemoptysis, fatigue
 - Signs: tachypnoea, tachycardia, end-inspiratory basal crackles, dullness to percussion over lung bases, S3, cardiomegaly, cyanosis, pleural effusion
- **Right HF**:
 - Due to:
 - Left Heart failure → pulmonary hypertension → RV failure
 - Cor pulmonale (R ventricle ↑ pressure due to disease of lung or pulmonary vasculature)
 - Constrictive pericarditis
 - Leads to:
 - Symptoms: fatigue, abdominal pain, oedema, anorexia, wasting, weight gain
 - Signs: enlargement of liver, spleen, kidneys, subcutaneous tissues and brain → ↑JVP, pulsatile liver, hepatomegaly, pitting oedema, ascites
- Congestive HF: both sides

Aetiology

- Age associated changes:
 - Reduction in β adrenergic responsiveness → ↓inotropic response and ↓vasodilation

- Increased arterial stiffness $\rightarrow \downarrow$ compliance $\rightarrow \uparrow$ afterload
- Alterations in cardiac filling: \uparrow connective tissue content of myocardium \rightarrow stiffer ventricle \rightarrow filling more dependent on atrial contraction $\rightarrow \uparrow$ pressure and size of left atrium \rightarrow predisposes to AF (\rightarrow further filling problems)
- Failure of reserve capacity of mitochondria
- Age associated diseases:
 - Hypertension \rightarrow risk factor for atherosclerosis, and \uparrow size and stiffness of left ventricle. By the time they have heart failure, may no longer have hypertension as they can't sustain the cardiac output necessary to be hypertensive
 - Coronary artery disease
 - Also \downarrow respiratory function and \downarrow renal function
- Precipitating factors unmask the subsequent reduced cardiac reserve, eg arrhythmia, infarction, AF, infection, thyroid disease, anaemia, PE, COPD \rightarrow hypoxia, DRUGS, etc
- Decreased perfusion due to decreased pump action $\rightarrow \downarrow$ kidney perfusion $\rightarrow \uparrow$ renin/aldosterone $\rightarrow \uparrow$ blood volume to try and increase pre-load and push heart up the Starling curve (however, they're often into negative marginal gain from increased volume). However, \uparrow BP also raises after-load and increases work of the heart $\rightarrow \uparrow$ ischaemia
- Cardiac dysfunction due to:
 - Disruption of circulatory system
 - Disorders of conduction
 - Lesion preventing valve opening
 - Pump failure (contraction/dilation) $\rightarrow \downarrow$ SV and \uparrow EDV $\rightarrow \downarrow$ CO
- Beriberi = heart failure due to deficiency of Vitamin B1 (Thiamine): bradycardia, premature ventricular beats, VF, AF, and heart block

Differential

- Must be able to prove the heart is the problem
- Otherwise consider:
 - Renal failure (eg nephritic syndrome) \rightarrow oedema
 - Liver disease or malnutrition $\rightarrow \downarrow$ albumin \rightarrow oedema

Investigations

- Bloods: FBC, Cr, electrolytes, Trop I, U&E, glucose, TFTs, LFTs, Cholesterol, ?ABG
- ECG
- CXR: although concomitant COPD may obscure changes in heart size and pulmonary vasculature
- Echocardiogram:
 - LV hypertrophy (normal thickness 1 cm), valve regurgitation or stenosis (check rate of flow), areas of hypokinetic myocardium
 - Normal velocity of blood through the heart = 1 m/sec. If aortic valve narrowed then faster flow then > 3 m/sec (same amount of blood through smaller space). Velocity between ventricles and aorta is proportional to the change in pressure
- Angiography

Treatment

- Principles:
 - Reverse underlying process (eg thyrotoxicosis)
 - Halt progression
 - Help symptoms
- Acutely:
 - Treat cause if any: hyperthyroid, hypertension, anaemia, alcohol, valve lesions
 - Symptomatic treatment:
 - Sitting position $\rightarrow \downarrow$ venous return
 - O₂ therapy (care with CO₂ retainers)
 - Frusemide 40 – 80 mg iv (if not already on it) $\rightarrow \downarrow$ afterload, vasodilation (\downarrow preload and \downarrow ECF volume). Watch for \downarrow K⁺
 - Morphine 5 – 10 mg iv: (as long as not low BP) a potent vasodilator (\downarrow preload $\rightarrow \downarrow$ work of heart and \downarrow pulmonary capillary pressure), bradycardic and sedative effects
 - Also consider:

- Aminophylline 250 mg over 5 – 10 min (+ive inotrope, mild diuretic, ↓bronchospasm. iv form of theophylline)
- Blood pressure control: Nitrates, Oral ACE inhibitors (↓preload and afterload, and ↑heart remodelling)
- Arrhythmia control: Digoxin, amiodarone
- Inotropes: dopamine, dobutamine
- DVT prevention
- Not β-blocker acutely, but ↑use in chronic management
- Intensive treatment:
 - Mechanical ventilation with positive end-respiratory pressure (CPAP) → ↓preload and ↑intra-alveolar pressure
 - Aortic balloon pump
 - Heart transplant
- Monitoring: weight, fluid balance, telemetry and U&Es (eg ↓K)
- **Chronic:**
 - Balancing act, especially in elderly: eg risks of polypharmacy, comorbid disease, what is the goal of treatment, postural hypotension if over-treated → falls, etc
 - Non-drug treatment:
 - Stop smoking
 - Control of blood pressure, DM, ↓alcohol
 - Exercise within ability to tolerate it (prevent further deterioration and problems of immobility)
 - Dietary advice: ↓weight, ↓Na and H₂O depending on weight (ie educate patient about illness and to monitor weight daily), low fat, high calorie
 - Physio: mobilisation and breathing control
 - Vaccination against influenza and pneumococcus
 - ‘Core’ drugs:
 - ACE Inhibitors: Drug of first choice in CHF. ↓dyspnoea, ↑exercise tolerance, ↓mortality, ↓admissions. Even if low blood pressure
 - Diuretics: for all people with volume overload and CHF. In elderly, effect of loop diuretics may be delayed through poor absorption, and ↓elimination → ↑effect. Accumulation can → deafness. Limited if poor renal perfusion. May exacerbate urinary incontinence. Low dose spironolactone may be useful (if high dose and ACE inhibitor → ↑K and ↓renal function)
 - Aspirin
 - Second line drug treatment for systolic dysfunction:
 - β-blockers, used cautiously, are gaining wider use:
 - If ↑sympathetic drive is causing a relative tachycardia then β-blockers will help (will get worse on β-blockers if reliant on sympathetic drive to maintain CO)
 - Criteria: chronic, stable, LV systolic impairment (ejection fraction < 45%), resting HR > 50 bpm, no contraindications (eg asthma, AV block). Not if very low ejection fraction
 - Start at low dose, titrate up as out-patient with carvedilol (α + β blocker) or metoprolol
 - Clear instructions to patient of symptoms of deterioration
 - See Clinical Use of Beta-Blocker Therapy in Patients with Heart Failure, Doughty RN and Richards AM, NZMJ, 9 Feb 2001
 - Spironolactone
 - Other Vasodilators (e.g. nitrates, calcium channel blockers) - ↓work of heart, ↑efficiency of heart, peripheral redistribution of blood. But problems with postural hypotension (especially if already volume depleted – check for hyponatraemia)
 - Inotropic agents if low BP, eg digoxin. Controversial in heart failure, main role is in AF
 - Limited role for anti-arrhythmic agents
 - Drug treatment for diastolic dysfunction (ie normal ejection fraction):
 - Avoid over diuresis
 - Tolerate AF poorly
 - Aspirin
 - β-blockers
 - Statins if cholesterol > 4 mmol/l

Myocarditis

- = Inflammation of the myocardium, excluding IHD

- Suppurative myocarditis: focal necrosis, pyogenic abscesses or diffuse spreading infection. Neutrophil infiltrate
- Interstitial myocarditis:
 - Characteristic of viral myocarditis
 - Occurs mainly in children and young women
 - Most have benign, self limiting course
 - Microscopic appearance: oedema, chronic inflammatory cells
- Parenchymatous myocarditis: diffuse, patchy destruction of muscle cells. Associated with diphtheria, typhoid, some β haemolytic streptococci, protozoa and parasitic infections
- Miscellaneous: Idiopathic (giant cell, Fiedler's). Also autoimmune disease or hypersensitivity to drugs

Cardiovascular Pharmacology

- For Anti-coagulation, see Anticoagulant Treatment, page 75

Idiot's guide

- Always push non drug treatment: lifestyle, smoking, etc
- Hypertension: Thiazides (not diabetics or gout) + β -blockers (not CORD/asthma). Maybe ACE inhibitors
- Angina: β -blockers + aspirin + nitrates. Maybe Ca channel blockers (\downarrow HR), statins, ACE (if hypertension/diabetes)
- Post MI: Aspirin, β -blockers, ACE if \downarrow LVF +/- statin
- Heart Failure: ACE + diuretic + aspirin. Maybe β -blockers, spironolactone, other vasodilators, statins, etc

ACE Inhibitors

- Block the formation of angiotensin II \rightarrow diuretic, \downarrow peripheral vascular resistance, and better tissue remodelling/healing of damaged myocardium. But 30% of hypertensives are non-responders
- Eg Captopril, quinapril
- Many patients (especially the elderly) don't respond on its own. Synergistic effect with diuretic (ie shifts ACE inhibitor dose-response curve to the left). If it's not working, add in a low dose diuretic
- Adverse effects:
 - Metabolic taste, hypotension (especially with first few doses), hyperkalaemia, angioedema, neutropenia, proteinuria.
 - \downarrow Renal function, especially if existing renal impairment (\uparrow efferent flow \rightarrow \downarrow glomerular filtration)
 - Dry cough (due to \uparrow bradykinins). If cough a problem, then use an angiotensin II receptor antagonist (eg Losartan)
 - Rash: may be long time after starting, especially captopril due to sulphur group
- Interactions:
 - Diuretics: hypotension + \downarrow renal function
 - NSAIDS: renal failure, hyperkalaemia
- Contra-indications:
 - Bilateral renal artery stenosis
 - Pregnancy, breast feeding
 - LV outflow obstruction (eg Aortic Stenosis)
 - Marked hypotension
 - Other drugs: K supplements, Li, NSAIDs
- Monitor for: \downarrow Na, \uparrow K, Cr > 200, rare neutropenia

Diuretics

- Common types:
 - Thiazides eg bendrofluazide. Flat dose response curve so \uparrow dose only \uparrow side effects. No \uparrow effect from a dose above 2.5 mg. Effect: mainly vasodilation, also inhibit Na/K co-transport in distal convoluted tubule \rightarrow salt and water loss. VERY cheap. Take 6 – 8 weeks to work
 - Frusemide: blocks Na/K/Cl transport in Loop of Henle. No role in lowering blood pressure
- Interactions:
 - General: NSAIDs, lithium, digoxin, ACE inhibitors, corticosteroids
 - Loop: antibiotics
 - Thiazides: calcium supplements

- Adverse drug reactions are dose dependent (\Rightarrow use in low dose):
 - General: dehydration, electrolytes, lipids, endocrine, skin
 - Loop: ototoxicity, $\downarrow K$, $\downarrow Ca$. Frusemide \rightarrow water rush. Difficult if you're out and about \rightarrow \downarrow compliance
 - Thiazide: $\downarrow K$, $\uparrow Ca$, $\downarrow Mg$, \uparrow urate (+/- gout), \uparrow lipids, progressive glucose rise over years, thrombocytopenia, impotence in high doses
- Spironolactone:
 - Acts at distal renal tubule as an aldosterone antagonist
 - Adverse effects: hyperkalaemia, diarrhoea, gynaecomastia
 - Interactions: ACE inhibitors, digoxin

β -blockers

- Action (effect takes 2 – 4 weeks):
 - Renal effect (\downarrow renin)
 - Pre-synaptic β -receptor blocker
 - \downarrow Cardiac output due to \downarrow rate and strength of myocardial contraction ($\rightarrow \downarrow O_2$ consumption). Acutely $\rightarrow \uparrow TPR$ (so not if peripheral vascular disease otherwise \uparrow ischaemia). $\downarrow CO$ resolves over time
 - ?Central action
- Use in angina, hypertension, heart failure
- Classified by:
 - Lipid vs H₂O soluble
 - β -receptor selectivity
 - α -blocking activity (eg labetalol \rightarrow prone to postural hypotension)
- Contraindications:
 - Arrhythmias: bradycardia and AV block
 - Asthma
 - Peripheral vascular disease: lead to unopposed $\alpha 1$ stimulation
 - Diabetes: block the symptoms of hypoglycaemia, potentiate effects of insulin and oral hypoglycaemics
 - Overt cardiac failure: negative inotropes – but still OK in heart failure at low dose
- Adverse effects (generally dose dependent):
 - Common: Lethargy, heavy legs (slowed up feeling due to $\downarrow CO$), cold extremities, \uparrow lipids, headaches, nightmares (in lipid soluble propranolol, not water soluble atenolol)
 - Less common: GI disturbances and rashes
 - Rapid withdrawal \rightarrow angina, arrhythmias due to $\beta 1$ up-regulation
- Interactions with:
 - Verapamil: severe bradycardia
 - Cimetidine: inhibits metabolism \rightarrow potentiates effect
- Consider α -blockers for hypertension – but not as first line agents (may exacerbate heart failure). Dilate peripheral arterioles (modern ones don't cause reflex tachycardia), less arterial dilation. Start low to avoid profound hypotension (especially elderly). Good for lipids

Ca Channel Blockers

- Uses: Angina, dysrhythmias, hypertension, NOT heart failure
- Hypertension: only in isolated systolic hypertension (eg due to hardened arteries)
- Not better than diuretics or β -blockers for hypertension, but additive effect
- Action: \downarrow myocardial work, decrease afterload, vasodilate coronary arteries
 - Verapamil (originally an anti-arrhythmic, derivative of theophylline, less effect on vasodilation but \uparrow bradycardia) and Diltiazem: slow conduction at the AV node and cause coronary vasodilation
 - Nifedipine: vasodilator \Rightarrow good for coronary artery spasm, but may also cause reflex tachycardia so may use with a β -blocker
- Adverse effects:
 - All cause headache, flushing, dizziness, hypotension, \downarrow LV function
 - Verapamil: constipation
 - Verapamil and diltiazem: \uparrow heart block
 - Nifedipine and verapamil: \uparrow blood sugar

- Interactions:
 - ↑ plasma digoxin levels
 - Enzyme inhibitors → ↑ plasma levels of carbamazepine and cyclosporin
 - Don't use verapamil with β-blockers: bradycardia + LVF
- Also consider long acting nitrates

Positive Inotropes

- Digoxin: only oral inotrope. Slows AV conduction and increases contractility
 - Use: in AF, slows rate → ↑ output. But poor for rate control – still ↑HR in response to standing up
 - Orally takes a week to reach steady state (T½ is 36 – 40 hours)
 - Shortens QT interval → causes digitalis effect on ST interval (not a sign of toxicity)
 - Low therapeutic index (although wide therapeutic range) → toxicity common:
 - CV: any *arrhythmia*, arrest, worsening heart failure
 - GI: anorexia, nausea, vomiting, diarrhoea, abdominal pain
 - CNS: headache, drowsiness, unsteadiness, blurred/yellow vision, *confusion*
 - Worse if:
 - Electrolyte disturbance: hypokalaemic, hypercalcaemia, alkalosis
 - Potassium sparing diuretics, steroids, verapamil, amiodarone, spironolactone
 - Disease: hypothyroidism, hypoxia, renal failure
 - Old age
 - Management: stop digoxin, check plasma level and K, treat arrhythmias, antidote (Digibind)
- Dopamine (precursor of nor-adrenaline)
 - In low doses → renal vasodilation and improved renal function
 - In higher doses → acts on cardiac β1 receptors → inotropic effects
- Dobutamine: acts on cardiac β1 receptors → inotropic effects

Lipid Lowering Drugs

- See Dyslipidaemia, page 30
- Lipids:
 - Cholesterol is most concentrated in LDL
 - HDL is beneficial
 - VLDL carries TAGs
- Hypercholesterolaemia:
 - Primary: Hepatic overproduction of VLDL → ↑VLDL/LDL/Remnant lipoproteins
 - Secondary: Obesity, diabetes, hypothyroidism, nephrotic syndrome, alcohol, drugs (oestrogen, Retinoids, β-blockers, thiazides....)
- Drug groups:

	Action	Effect
<i>HMG Co-A Reductase Inhibitors:</i>		
Statins		
Simvastatin, Pravastatin, Atorvastatin	↓Cholesterol synthesis	LDL ↓ 20 – 40% HDL ↑ 5 – 15% TAG ↓ 10 - 20
<i>Fibrin-acid derivatives:</i>		
Benzafibrate, Gemfibrozil	↑Lipoprotein lipase activity. ↓release of FFA from periphery	LDL ↓ 10 – 15 % HDL ↑ 10 – 15 % TAG ↓ 20 – 50%
<i>Bile Acid Sequestrants:</i>		
Cholestyramine, Colestipol	Non-specific binding of bile acids	LDL ↓ 15 – 30% HDL ↑ 3 – 5% TAG: no affect (but can rise)
<i>Nicotinic acid derivatives:</i>		
Acipimox	↓VLDL. ↓FFA from periphery	LDL ↓ 10 – 25 HDL ↑ 15 – 35 TAG ↓ 20 - 50

- Commencement of treatment depends on HDL:cholesterol ratio plus other risk factors

- HMG-CoA Reductase Inhibitors (Statins):
 - Treatment: Requires health benefits approval (it's expensive) and is always accompanied by diet
 - More effect in lowering plasma concentrations of LDL and total cholesterol → ↓mortality in hypercholesterolaemia + angina
 - SE: rare. GI, headaches, ↑LFTs, myopathy from ↑Ck. Potentiates warfarin
- Fibrates: ↑HDL and ↓TAGs
- Bile-acid sequestrants: Indicated for children and women of childbearing age. SE: constipation, skin rashes. Bind fat soluble vitamins and other drugs (eg warfarin, give two hours before or 4 hours after)

Cardiomyopathy

- = Primary or idiopathic diseases involving the myocardium. Diagnosed by excluding other more common causes of heart failure: IHC, hypertension, rheumatic fever, and infectious myocarditis

Primary Cardiomyopathy

Congestive-Dilated Cardiomyopathy

- Presents as congestive heart failure at any age
- Men twice as common as women
- Exclude pre-existing hypertension and alcoholism
- Macroscopic appearance: greatly dilated ventricles, heart weighs 500 – 1000g (normal is 300g female, 350 g male)
- Microscopic appearance: patchy interstitial fibrosis, ↑↑interstitial oedema, hypertrophy of remaining fibres
- Complications: arrhythmia, mural thrombus, mitral and tricuspid insufficiency
- Prognosis: progressive disease, no cure

Hypertrophic Cardiomyopathy

- Disproportionate hypertrophy of the interventricular septum → ventricular outflow obstruction
- Familial and non-familial forms
- Macroscopic appearance: heart weighs 600 – 1300g. Septum thicker than free wall of left ventricle
- Microscopic appearance: diffuse hypertrophy of tangled myocytes. Interstitial collagen
- Prognosis: poor. 1/3 die from outlet obstruction (can be precipitated by digoxin)

Restrictive Cardiomyopathy

- Endocardial fibroelastosis: cartilage-like thickening of the left sided endocardium. Most common < 2
- Endomyocardial fibrosis: Only tropical Africa. Fibrosis → thickening of chordae tendinae and aortic valve leaflets

Secondary Cardiomyopathy

- Alcohol, cobalt, sarcoid (infiltrative granulomatous), amyloid (accumulation of insoluble β pleated proteins derived from immunoglobulins in elderly patients), metastatic carcinoma, storage diseases (eg haemochromatosis), ischaemia
- Effect of alcohol on the heart:
 - Binge drinking (also exercise and caffeine) → AF a day later lasting for a day
 - Fibrotic cardiomyopathy
 - Arrhythmia

Neoplasia of the Heart and Blood Vessels

- Haemangioma:
 - Common congenital vascular lesions usually occurring in the skin
 - Haemangioendothelioma: endothelial vascular tumour, intermediate between haemangioma and frankly malignant angiosarcomas
 - Multiple Haemangiomatic syndromes: angiomatic lesions present in two or more tissues
- Kaposi's sarcoma: malignant tumour of endothelial cells. Associated with AIDS. Painful purple to brown lesions
- Myxoma: most common primary benign tumour of the heart. Jelly like appearance, typically located on the atrial side of the mitral valve

- Rhabdomyoma: primary benign striated muscle cell tumour of the myocardium, typically found in children

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Physiology

- For acid-base disturbances, see Acid-Base balance, page 113

Blood Gases

- Normal Values:
 - PaO₂: 75 – 100 mmHg, 10 – 13.3 kPa. Dependent on ventilation/perfusion balance (A-a gradient) and inspired O₂ concentration
 - O₂ saturation: 95 – 100%
 - PaCO₂: 36 – 46 mmHg. If high then hypoventilation, if low then hyperventilation. Measured with a capnograph. pH falls by 0.1 for every rise of 10 CO₂
 - Plasma HCO₃ (arterial): 22 – 26 mmol/L
 - To convert mmHg to kPa divide by 7.5 (multiply by 0.133)
- PAO₂ is lower than inspired PO₂ because:
 - It becomes saturated with water vapour
 - It is diluted by expired CO₂
 - O₂ is absorbed into the blood
- Factors affecting the A-a gradient (normally 5 mmHg at FIO₂ of 21%, may be up to 100 at 100%):
 - Ventilation/Perfusion balance (V/Q): most common cause of a fall. Responds well to O₂ therapy
 - Diffusion
 - Shunts (pathological or anatomical)
- Calculating the A-a gradient:
 - PIO₂ = (PB – PH₂O) * FIO₂ = (760-47) * 21% = 150 mmHg
 - PAO₂ = PIO₂ – PaCO₂/R
 - A-a gradient = PAO₂ – PaO₂. Normal is 5 – 15
- Saturation = % of haemoglobin that is fully bound. Determined by PO₂ and shape of dissociation curve
- Oxyhaemoglobin dissociation curve
 - Shifted right by ↑blood temp, CO₂, H⁺, 2,3BPG
 - Shifted left by ↓blood temp, CO₂, H⁺, 2,3BPG
- O₂ available to tissues (Oxygen flux) depends on:
 - O₂ saturation
 - Hb concentration
 - Blood flow
 - Normal flux is 1000 ml/min. If flux falls below 250 then hypoxia
- Cyanosis:
 - Peripheral cyanosis: capillary de-oxy Hb > 50 g/litre. Eg due to being cold and vasoconstricted
 - Central cyanosis: due to ↓saturation and de-oxy Hb > 50 g/litre eg in mouth and tongue

Lung Function Tests

TLC Total Lung Capacity	(S)VC (Slow) Vital Capacity	IC: Inspiratory Capacity	
	FRC: Functional Residual Capacity		Vt: Tidal Volume
	RV: Residual Volume		RV: Residual Volume

- Definitions:
 - PEFR = peak expiratory flow rate
 - FEV_{1.0} = maximum volume of air that can be exhaled during the first second of a Forced Vital Capacity (FVC= maximum expired volume = FV). May use SVC if its higher
 - Normally 80% of FVC
 - < 75% ⇒ obstructive lung disease
 - > 75% ⇒ restrictive lung disease, eg lung fibrosis, neuro-muscular disease, chronic PEs (→ scarring) and heart failure
 - But this can lead you astray. Eg if bronchodilator → ↑FVC by more than FEV, then the ratio drops
 - FEV 25-75%: Mean forced expiratory flow from 25 to 75% of vital capacity = Mean Mid-expiratory Flow (MMEF). Gets rid of peak flow which is very effort dependent → more reliable measure

- VC = vital capacity:
 - FVC: forced vital capacity
 - SVC: slow vital capacity
- FIF50%: Forced inspiratory flow at 50% of vital capacity
- PIFR: Peak inspiratory flow rate
- Patterns:

	Obstructive	Restrictive
FEV1	↓↓	↓
FVC	↓	↓↓
FEV/FVC	↓	↑
TLC	↑	↓
RV	↑	↓
DLCO	↓	↓

- Diffusing Capacity: DL CO: Diffusing capacity of the lung for Carbon Monoxide (needs adjustment for Hb – eg anaemia, polycythaemia)
- Performing Lung Function Tests:
 - Requires at least 3 manoeuvres, the best two having FEV1.0's and FVCs within 5% of each other
 - Biggest problems with serial reproducibility are obtaining maximum inspiration first, and getting maximum effort
 - All are reported at BTPS (body temperature, saturated)
 - If assessing broncho-dilator responsiveness, should have no inhaler for 2 hours before hand. Maximum responsiveness usually 20 minutes after dosing
 - Predicted values are based on age, height and sex. Different racial groups and people with varying proportions (eg long legs/short torso) may be very poorly approximated by predicted values
 - Flow-volume Loop gives very valuable information. Eg in emphysema, ↓↓ expiratory flows but inspiratory flows normal
- Patterns of disease:
 - Obstruction: ↓flow
 - Restrictive: ↓volume
- Other lung function tests:
 - Asthma provocation: for pilots, divers, police, etc
 - Cardiopulmonary exercise testing – finds how much of shortness of breath is due to pulmonary causes and how much to cardiac causes

Respiratory Failure

- Ventilatory failure: When bellows function inadequate to excrete CO₂ produced (ie above 60 mmHg)
- Respiratory Failure: (PaO₂ < 60 mmHg)
 - Type 1: PaCO₂ < 50 mmHg ⇒ VQ mismatch (less O₂ absorbed in hypoperfused areas, hyperperfused can't compensate due to the sigmoid shape of the dissociation curve) **plus** other causes (e.g. heart failure)
 - Type 2: PaCO₂ > 50 mmHg ⇒ hypoventilation – both gases are affected reciprocally – only lung problem can cause this
- Respiratory Failure can be due to:
 - Central respiratory depression:
 - Drugs: opiates, alcohol, barbiturates
 - Brain stem: CVA, coning
 - If A-a gradient normal but patient hypoventilating ⇒ central depression. If young then ?OD
 - Sleep Apnoea syndromes
 - Lung Pump Failure: neuromuscular disease, chest wall, lung disease. E.g. diaphragm dysfunction:
 - Unilateral paralysis may be asymptomatic
 - Bilateral paralysis: neurological (e.g. polio, motor neuron, Gillian Barre) or myopathic (e.g. hypothyroid)
 - Signs: orthopnea, morning headache (hypercapnia over night), paradoxical breathing (chest wall and abdomen go in opposite directions when breathing), lung function worse when lying down
 - Treatment: treat cause, positive pressure ventilation systems

Oxygen Therapy

- Ensure PO₂ is on plateau of O₂ saturation curve (ie PaO₂ > 70 mmHg)
- Shunt is resistant to O₂ therapy, whereas a diffusion abnormality and V/Q mismatch respond well
- Complications:
 - Reduced respiratory drive in CORD. Consider if ↑PCO₂ but pH not as low as you'd expect.
Don't give too much O₂ otherwise ↓respiratory drive → ↑CO₂. Aim for saturation of ~ 90%
 - Loss of nitrogen splint, etc
- Levels of O₂ therapy:
 - 21%: Room air
 - 24%: nasal prongs at 1 litre
 - 28%: nasal prongs at 2 litres
 - 32%: nasal prongs at 3 litres
 - 35%: Hudson mask at 6L O₂/min
 - 40%: Hudson mask at 8L O₂/min. Maximum level obtainable with a mask (inspiratory flow > flow from wall)
 - 50%: Hudson mask with rebreather bag
- Types of ventilation:
 - CPAP: Continuous positive airways pressure – splints airways open at end of respiration
 - BiPAP: Positive pressure for inspiration only. Good if CO₂ retention – makes it easier to blow off CO₂
 - IPPV = intermittent positive pressure ventilation: complete control
 - PEEP = positive end expiratory pressure ventilation: splints collapsed or fluid filled alveoli
 - Complications of ventilation:
 - Application of pressure to lungs → rupture, ↑thoracic pressure → ↓venous return
 - Artificial airway → obstruction, trauma to teeth, pharynx, cilia damage, infection
 - Ventilation mismanagement → inappropriate ventilation, hypoxic gas mixture, equipment failure

Respiratory History

- See Differentiating Chest Symptoms, page 16

Respiratory Exam

- For Chest X-ray, see Chest X-ray, page 27

*Inspection, Palpation and Percussion **

- Inspection:
 - Count respiratory rate (at rest should be < 14 per minute)
 - Chronic airways disease → barrel (expanded chest) → can't find apex beat
 - Look for use of accessory muscles. Are intercostals depressed (ie being used a lot)? Look for paradoxical breathing of the abdomen
 - Cyanosis (eg tongue)
- Ask patient to cough. Listen for wheeze, gurgling, etc
- Inspect sputum
- Listen for stridor or hoarseness (laryngitis, cancer affecting left recurrent nerve or larynx)
- Hands:
 - Clubbing (and maybe Hypertrophic Pulmonary Osteoarthropathy – 'swollen' metacarpals and elsewhere, eg in lung cancers). See Hands, page 7 for causes of clubbing
 - Staining from cigarettes
 - Wasting (Pancoast tumour)
 - Pulse rate: tachycardia
 - Flapping tremour: late and unreliable sign of severe CO₂ retention
- The face:
 - Eyes for Horner's syndrome (constricted pupil, partial ptosis)
 - Tenderness over sinuses → sinusitis
 - Nose: check for polyps (associated with asthma), deviated septum (nasal obstruction), etc
 - Throat for URTI
 - Check lymph nodes

- Trachea:
 - Check for displacement
 - Tracheal Tug: trachea moves inferiorly with inspiration, due to over expansion of the lung in airflow obstruction
- Chest:
 - Inspect:
 - Shape and symmetry, including funnel chest (= pectus excavatum or sunken sternum), kyphosis (forward curvature) and scoliosis (lateral bowing)
 - Scars, signs of radiotherapy
 - Subcutaneous emphysema – crackling under the skin due to air from pneumothorax
 - Prominent veins in SVC obstruction
 - Movement when breathing in and out – better from behind. Look for uni-lateral or bi-lateral reduction in movement
 - Palpation:
 - Check expansion: the affected side does NOT expand – regardless of pathology
 - Apex beat: if not found then → ?hyper-expanded. Maybe displaced by pathology (pneumothorax, fibrosis, etc)
 - Vocal fremitus: Feel with hand while patient says 99, each side front and back
 - Compress sternum to spine → pain if fracture or bone tumour
 - Percussion:
 - Ask patient to move elbows forward to move scapula off the lungs
 - Around lung and also directly on the clavicle
 - Normal lung is resonant, pneumothorax is hyper-resonant, liver is dull, consolidation is dull, effusion is stony dull

Chest Sounds

- When auscultating, ask patient to breath through mouth – not to take deep breaths

	Vesicular breath sounds (= normal breathing)	Bronchial breathing
Length	Inspiration > expiration (inspiration requires work, expiration is elastic recoil – snaps back)	Inspiration =< Expiration (takes longer for air to get passively squeezed out through reduced bronchioles)
Relative Volume Gap between in and out	Inspiration louder No	Equal (sounds like Darth Vader) Yes

- Crackle:
 - = Crepitations
 - Coarse or fine (like hair rubbing)
 - Short, discontinuous, non-musical sounds heard mostly during **inspiration**
 - Fine (high pitched) are from distal air-spaces, coarse (low pitched) are proximal air spaces
 - Produced when there is fluid inside a bronchus with collapse of the distal airways and alveoli
- Wheeze
 - = Rhonchi, rhonchus, rale
 - Continuous musical sounds heard mostly during **expiration**
 - Produced by airflow through narrowed bronchi
 - Narrowing may be due to swelling, secretions, spasm, tumour, or a foreign body
- Pleural Rub
 - Grating sound like Velcro ripping or walking on snow on **inspiration and expiration**
 - Produced by motion of roughened or thickened pleura
 - Caused by inflammatory or neoplastic cells or fibrin deposits

- Differentiating Consolidation from Pleural Effusion
 - Consolidation = exudate into alveoli. Signs are:
 - Expansion: reduced on affected side
 - Vocal resonance and tactile fremitus (patient says '99' and listen with stethoscope/feel with hand): ↑ on affected side
 - Percussion: dull but not stony dull
 - Breath Sounds: *increased volume* and bronchial not vesicular (ie will hear coarse breath sounds like over the trachea)
 - Additional Sounds: inspiratory crackles (as pneumonia resolves)
 - Vocal Resonance: increased
 - Plural Rub: may be present
 - Effusion = fluid in pleural space (but not blood – that's haemothorax, and not pus – that's empyema). Signs of effusion are:
 - Displaced trachea if massive effusion
 - Expansion: reduced on affected side
 - Percussion: stony dullness over effusion
 - Breath Sounds: *reduced* or absent
 - Vocal Resonance: reduced
 - The key differences are therefore:

	Consolidation	Effusion
Percussion	Dull	Stony Dull
Breath Sounds	Bronchial	Reduced
Vocal Resonance	Increased	Reduced

- Common presentations:

	Expansion	Percussion	Breath sounds	Vocal Resonance	Trachea
Consolidation	↓	Dull	↑, Bronchial, course crackles	↑	-
Effusion	- or ↓	Stony dull	↓	↓	-
COPD	Hyper-expanded	Hyper-resonant	Wheeze	-	-
Pneumothorax	- or ↓	Hyper-resonant	↓	↓	Deviated if tension
PE	-	- (unless effusion)	-	-	-
Fibrosis	↓	- or dull	Crackles	↑	Depends
LV Failure	↓	Dull	Fine crackles	-	-
Collapse	↓	Dull	↓	↓	Deviated

Other systems *

- Check JVP for right heart failure
- Listen to P2 of second heart sound, at 2nd intercostal space on the left. If louder → ?pulmonary hypertension
- Check liver for tumour 2nd to lung cancer, and for 'ptosis' – displaced downwards in emphysema
- Pemberton's sign: SVC obstruction – hold arms over head → facial plethora, inspiratory stridor and ↑JVP
- Feet: check for oedema (pulmonary hypertension) and DVT

Upper Respiratory Tract

- See also URTI in Respiratory Tract Infections in Children, page 605

Nasal & Sinus

- For Nasal neoplasms, see Cancer of the Nasal Cavity and Paranasal Sinuses, page 86
- Warms, cleans and humidifies inspired air. By back of nose air is 98% humidified and 35 C
- Anatomy: maxillary, ethmoid, frontal and sphenoid sinuses. Concha and turbinate bones

Nasal obstruction

- Mechanical:
 - Defect in cartilage or bone
 - Septal deviation. Overtime → paradoxical obstruction – hypertrophy of turbinate on other side → bilateral obstruction. Treatment: septoplasty
- Mucosal:
 - → Blocked nose, mucoid discharge, ↓smell
 - Vasomotor rhinitis (VMR): there is normally a cycle between one nostril blocked and other cleared. This cycle upset. Treatment: cauterise turbinates → reduce venous congestion
 - Allergic rhinitis
 - Polyps: sessile or pedunculated. Usually inflammatory – related to asthma and aspirin sensitivity. Can be idiopathic or secondary to infective sinusitis
 - Treatment: topical steroids (↓allergy, ↓primary polyps, ↓VMR), antihistamines, mast cell stabilisers

Epistaxis

- Kids: from Little's area (= Kiesselbach's area). Anterior septum. Naso-palatine plexus. Treatment: cauterise
- Adults: From further back – septal or lateral wall. In elderly, mortality from severe epistaxis 1% - from secondary effects eg stroke (aspirin common cofactor → ↑bleeding)

Sinusitis

- See also Acute Sinusitis, page 608
- Face pain after cold
- Maxillary most common presentation, although ethmoid more commonly infected
- Causes: Strep pneumoniae, Strep pyogenes, H. influenzae, B. catarrhalis
- Treatment: Amoxil
- Complications:
 - Orbital cellulitis via orbital periosteum → optic nerve compression → compression of ophthalmic artery → retinal blindness. Need to drain pus and iv antibiotics
 - Sphenoidal and frontal sinusitis can → cerebral complications (eg cavernous thrombosis)
- Chronic sinusitis: puss, ↓smell, no pain. Can be from dental infection

Allergic Rhinitis

- See also Allergy and Hypersensitivity Disorders, page 309
- Symptoms: Recurrent or acute
 - Sneezing, blocked or runny nose, itchy watery or puffy eyes, itchy throat
 - May also be epistaxis, snoring, mouth breathing
- Examination: look at anterior nares for nasal patency, polyps (chronic rhinitis), secretions, oedema
- Two types:
 - Seasonal Allergic Rhinitis = Hay fever. Allergy to birch or grass pollen etc. especially rye grass
 - Perennial Allergic Rhinitis: allergy to dust mites, cat dander, moulds, etc
- Non-drug treatment:
 - Avoid allergen
 - Avoid other irritants: perfume, temperature change, other smoke
- Drug treatment:
 - Antihistamines: Some can cause sedation, especially if taken with alcohol
 - Decongestants: Vasoconstrictors. Can have stimulant effects (including ↑BP). Overuse → rebound congestion
 - Mast cell stabilisers: Nasal spray. Slow onset
 - Topical nasal steroids: Slow onset. Can cause mucosal atrophy → nose bleeds
 - Desensitisation: Injections of increasing doses of allergen. Expense and takes time (eg up to two years)

Acute Pharyngitis

- See also Pharyngitis, page 607
- Clinical signs: fever, respiratory distress, cervical lymphadenopathy, pharyngeal erythema, pharyngeal exudates

Causal Organisms

- Viral causes (commonest):

Agent	Disease	Symptoms
Rhinovirus, coronavirus	Common Cold	Common cold. Fever uncommon except in kids
Influenza (A & B)	'Flu	As for common cold + fever, headache, generalised myalgia
Parainfluenza virus 1-3	Croup = Laryngotracheobronchitis	Initial: sore throat, rhinorrhoea, mild cough Leading to: severe cough (seals bark), hoarseness, inspiratory stridor (subglottic inflammation)
Adenovirus	Pharyngo-conjunctival fever	Sore throat (often erythema <i>and exudate</i> – even though virus), fever, headache, myalgia, conjunctivitis
Herpes Simplex		Mild: indistinguishable from other viral URTI. Severe: pharyngeal exudate/erythema, shallow ulcers, vascular rash on lips
Epstein Barr Virus	Infectious Mononucleosis – Glandular fever (See Epstein Barr Virus, page 505)	Usually adolescents/young adults. Sore throat (erythema/exudate in 50%), fatigue, malaise, fever, headache, cervical lymphadenopathy, atypical mononucleosis on blood film, splenomegaly

- Bacterial Causes:

Agent	Disease	Symptoms
Streptococcus Pyogenes (Lancefield Gp A) & Strep Group C	Pharyngitis/Tonsillitis	Marked variation: Mild: indistinguishable from viral URTI, minimal erythema. Severe: Marked pharyngeal erythema & florid tonsillar exudate, high fever, cervical lymphadenopathy, leucocytosis on blood film. Type M strains → Rheumatic fever.
Mixed anaerobes	Gingivitis/Pharyngitis	Polymicrobial infection, due to poor dental hygiene, bad breath
Corynebacterium diphtheriae	Diphtheria	Pharyngeal diphtheria rare. Range from mild non-specific illness to severe. Sore throat/fever, pain on swallowing, headache, vomiting. Characteristic greyish-green membranous exudate on pharynx
Neisseria gonorrhoeae	Pharyngitis	Mostly asymptomatic. Mild pharyngitis. Pain/difficulty swallowing

- Fungal causes:

Agent	Disease	Symptoms
Candida Albicans	Thrush	Usually immunocompromised. Creamy white plaques on tongue/mucosa. Complication of asthma steroids and long-term antibiotics

Diagnosis

- Throat swabs:
 - For routine bacterial culture: especially to confirm/exclude Strep Pyogenes
 - Low sensitivity (?30%) and specificity (?75%)
 - 40 – 50% of people with sore throats have bacteria isolated
 - Lots of variability: swab-taking technique, delays in transport, etc
 - Worth it for \$18?
- Nasopharyngeal washings (kids): Antigen detection by immunofluorescence for RSV, Influenza A & B, Parainfluenza 1 – 3 and adenovirus

Other URTIs

Infection	Common causative organisms
Acute Otitis Media	Strep pneumoniae, H influenzae, Branhamella catarrhalis. See Acute Otitis Media, page 605
Acute Sinusitis	Strep pneumoniae, H influenzae
Acute Epiglottitis	H influenzae type B. See Epiglottitis, page 609
Chronic Bronchitis (acute infectious exacerbations)	Strep pneumoniae, H influenzae, Branhamella catarrhalis
Bronchiolitis	Respiratory Syncytial Virus. See Bronchiolitis, page 610

Antibiotic Treatment of URTI

- See also Acute Otitis Media, page 605
- Treatment for Strep Pharyngitis (Path lecture):
 - Oral Penicillin:
 - On empty stomach (before food)
 - 500 mg (200 for kids) 8 hourly for 10 days (adults)
 - If compliance in doubt, IM benzathine penicillin G (single dose)
 - Allergic to Penicillin: Erythromycin 500 mg (200 for kids) 8 hourly for 10 days
- Antibiotic treatment (source – ‘Just Say No’, Thomas and Arroll, NZMJ, 14 July 2000):
 - No benefits in patients with colds
 - Trivial benefit in patients with acute bronchitis
 - Trivial benefit in all but a minority of patients with acute exacerbations of COPD
 - Modest benefit in sinusitis
 - But, in real life, antibiotics are prescribed for a majority of patients with URTI
- Antibiotic treatment (Cochrane review):
 - Absolute benefits modest
 - Preventing complications can only be achieved by treating many who will derive no benefit
 - Symptoms: reduced duration by about half a day, especially at 3 days (although 50% of untreated had also settled by then)
 - Non-suppurative complications: Reduces rheumatic fever to less than one third. Possible protection against acute glomerulonephritis (although rare)
 - Suppurative complications: Reduces rate of otitis media to a quarter (NNT = 29), acute sinusitis to about one half and reduced incidence of quinsy
- No risk of delaying antibiotic treatment for possible Strep Pyogenes pharyngitis until culture results received. Late treatment as effective as early treatment
- Risks of ‘over treatment’ with antibiotics: Penicillin resistance – 2 to 9 times, ↑ risk of subsequent otitis media, pneumonia, bacteraemia or meningitis being caused by resistant S. Pneumoniae. ‘Cherish your normal flora and don’t assault it with antibiotics’
- Delayed/contingent prescription can allow ↓ antibiotics without ↑ morbidity. Eg antibiotics dispensed for sore throat dropped from 99% to 31% with wait of 2 days
- For Treatment of Otitis Media, see Acute Otitis Media, page 605

Larynx

- See also Tumours of the Larynx, page 86
- Function: protect airway from saliva and food, voice production
- Vocal chords shut during coughing, straining, lifting → maximal splinting from thoracic muscles
- Anatomy:
 - Recurrent laryngeal: maintains open vocal chords via abductor muscle. If damaged → stridor.
Rest of muscles supplied by superior laryngeal nerve

- Pharynx: superior, middle and inferior constrictor muscles attach on the cervical spine at medium raphae
- Paediatric problems:
 - See also Neonatal Acute Airway Problems, page 595 and Respiratory Illness, page 604
 - Signs: stridor, feeding difficulties
 - Failure of canalisation → severe (normally dies)
 - Laryngomalacia: Supra glottic structures floppy → collapse on inspiration → inspiratory stridor. Improves with ↑ muscle tone/innovation
 - Subglottic stenosis: congenital or trauma (eg too big a ventilation tube)
 - Croup:
 - = Laryngo-tracheo bronchitis.
 - Inspiratory and expiratory stridor, barking cough
 - If frequent, may have anatomical narrowing
 - Usually viral infection. If severe, steroids → ↓ inflammation
 - Obstructive sleep apnoea:
 - Very different to adults: usually due to enlarged adenoids/tonsils – snore loudly
 - → Failure to thrive, behavioural problems, etc
 - Obstructive apnoea up to age 7 → take adenoids out
 - Epiglottis:
 - Symptoms: obstruction, sore throat, drooling, toxic/septicaemia
 - Cause: bacterial infection (eg H. Influenzae)
 - Medical emergency: can deteriorate quickly. Don't examine throat – may cause spasm and obstruct
 - Emergency treatment: Geudal airway and ambubag. If unsuccessful get a very experienced person to intubate. If unsuccessful cricothyroidotomy with 14 gauge needles
- Tonsillitis:
 - Tonsils are not normal lymph nodes: don't have capsule or afferent vessels
 - Bulk of lymphoid tissue is in base of tongue
 - Decrease in size with age. At 40 half the size as when 15
- Foreign bodies:
 - Can't eat or drink.
 - In kids: 10-cent pieces, inhaled peanuts. Differential: asthma (cough and wheeze). If < 2 years old, do CXR and look for collapse distal to obstruction
 - In elderly with dentures: can't chew or feel unwell
 - Must take out: if stuck in gullet, will perforate within 7 days. Can linger for months in lung
- Vocal chords:
 - Papillomas: usually solitary. Very low incidence of malignant change. Laser them (usually repeatedly)
 - Nodules: usually bilateral. Keratinised lesions from chords banging together. Treatment: vocal rest, correct voice abuse
 - Polyps: usually unilateral. Granulation tissue/inflammatory
 - Reincher's disease: in middle aged female smokers. Degenerative, gelatinous polyps of surrounding mucosa → hoarse voice, obstruction. Cause unknown
- Recurrent Laryngeal Palsy:
 - Usually left nerve: longer. Right only goes round subclavian
 - 40% idiopathic
 - Exclude: bronchogenic cancer, mediastinal lymph nodes (eg lung or breast Ca), Ca of larynx, mononeuropathic infection
- Voice disorders (Dysphonia, Aphonia):
 - Obstruction to vocal chord closure: vocal chord thickening/oedema, nodules, papilloma, ulcers, polyps
 - Larynx growths: leukoplakia, hyperkeratosis
 - Trauma: intubation, external
 - Paralysis: superior or recurrent laryngeal nerve
 - Vocal hyperfunction: spastic dysphonia, tension due to voice abuse (singers, teachers)
 - Presbyphonia: in the elderly
 - Other: chronic laryngitis → mucosal atrophy, Parkinson's, Motor neuron disease, following laryngectomy

- In all cases refer to speech-language therapy for assessment/management

Adult Pneumonia

- = Inflammation and consolidation of the pulmonary parenchyma

Classifications

- Community acquired vs. hospital acquired
- Typical vs. atypical organisms
- Lobar vs. diffuse/non-lobar/bronchopneumonia (although no clinical relevance as it doesn't tell you which bug)
- Normal vs. immunocompromised
- Severe or not
- Includes: bronchopneumonia, lobar pneumonia, interstitial pneumonia, and infectious granulomas

History

- Previous pneumonia, asthma, bronchitis
- Aspiration risk
- Social History: smoking, alcohol, occupational or hobby exposure (birds, dust, healthcare worker, etc)
- Infectious: overseas travel, recent arrival
- TB History: race, previous history, family history, exposure, living situation, BCG status
- History or immuno-suppression: transplant, cancer, high dose steroids, HIV risk (sexual, weight loss, night sweats)

Epidemiology

- 10% of hospitalisations
- At risk:
 - Infants and children: more frequent exposure, immature immune system, narrower bronchial tree
 - Elderly
 - Altered level of consciousness: post-operative, CVA, fits, drugs/alcohol, diabetic coma: diminished cough reflex
 - Smokers
 - Patients with pulmonary oedema
 - Immune deficiencies: leukaemia, lymphoma, renal transplant patients, cytotoxic drugs
 - 80% of AIDS patients die of respiratory failure: 60% of these will have a pulmonary infection

Types of Infectious Pneumonia

Bronchopneumonia

- Patchy consolidation of the lung. Infection centered on a bronchus or bronchiole, involving immediately adjacent alveoli. Pleura not usually involved. Can overlap with lobar pneumonia.
- Infection is spread through the airways
- Macroscopic appearance: patchy consolidation – firm, raised, nodular, red to grey-white. Colour varies with the amount of necrosis and haemorrhage, and due to stage. May involve one or more lobes
- Microscopic appearance:
 - Bronchocentric lesions
 - Early: congestion and oedema
 - Progresses to: neutrophils + proteinaceous (fibrinous) exudate + RBCs fill distal airways and alveoli.
 - Resolution: airways clear but may organise into fibrous tufts. Parenchymal destruction depending on organism
- Causative organisms:
 - Depends on whether community or hospital acquired, depressed pulmonary defences, etc
 - G +ive cocci (staphs and streps) and G -ive H Influenza, Pseudomonas, E Coli and Klebsiella
 - S. Aureus and G -ives more common in hospital acquired (eg in ICU) – also more destructive
 - Pseudomonas aeruginosa: can infect lung haematogenously → infection of vascular walls → haemorrhagic pneumonia. Common in burn, immunocompromised and cystic fibrosis patients. Usually fulminant course
 - Legionella pneumonia: characteristic morphology is acute fibrino-purulent exudative pneumonia – neutrophils + macrophages within a fibrinous exudate. Inflammatory response spares alveolar

walls, so no necrosis or haemorrhage. Mild and self-limiting, except in elderly and smokers. 10 – 20% mortality in immunocompromised. Rumoured to have prominent GI symptoms (diarrhoea and vomiting) – but ?any difference in incidence to other agents. Characteristic in air conditioning (ie plumbers, office workers, etc) and carriage in potting mix (ie gardeners).

Lobar pneumonia

- Involves whole lobe uniformly, often with reactive fibrinous pleuritis
- 95% of cases are Strep pneumoniae
- Pathogenesis: bacteria inhaled → profuse fluid exudate (good growth medium) → infection spreads through interalveolar pores throughout lobe
- Macroscopic and Microscopic appearance: 4 stages based on macroscopic appearance:
 - Congestion: 12 – 24 hours, oedema
 - Red hepatisation: 2 – 3 days. Redness due to congestion and haemorrhage. Fibrinous neutrophilic exudate, consistency of liver
 - Grey hepatisation: 3 – 4 days, grey due to ↑WBCs and fibrin, and ↓blood due to compression of capillaries
 - Resolution: 2 – 5 days, macrophage phagocytosis and clearance. Pulmonary architecture usually maintained, or fibrous tufts fill distal airways and alveoli and are then incorporated in the interstitium → interstitial fibrosis
- Complications: 20 – 30% get bacteraemia → meningitis, endocarditis, arthritis, etc.
- Presentation: fever, chills, productive cough with sputum from watery to rusty as the disease advances. ↓Functional parenchyma → SOB and cyanotic. Pleural rub.

Lung Abscesses

- Can occur secondary to pneumonia or independently. There are two patterns:
 - Multiple abscess: haematogenous spread or bronchopneumonia from a virulent organism that causes necrosis
 - Solitary abscess: usually due to anaerobic organism – eg following aspiration in alcoholic with depressed reflexes

Infectious Granulomas

- Three possibilities for a granuloma:
 - Tb: no neutrophil infiltrate in granuloma → caseating necrosis
 - Fungal: causes abscess ⇒ neutrophils/puss in the middle
 - Sarcoidosis: non-necrotising (non-infectious)
- Mainly Mycobacterial Tuberculosis: can infect any organ but commonly the lung
- Immune cells in granulomas:
 - Histiocyte = epithelioid cell = macrophages ('eating phase' as opposed to circulating in blood when its called a monocyte)
 - Bigger and more cytoplasm than a lymphocyte
 - If cytoplasm fuses → giant cell with multiple nuclei

Tuberculosis

- See also Mycobacteria, page 502
- Usually *Mycobacterium Tuberculosis*. In AIDS, may be *M. avium-intracellulare*. *M. bovis* causes GI Tb in 3rd world from contaminated milk
- Epidemiology:
 - Affects 33% of world's population and causes 3 million deaths a year.
 - In first world, improved sanitation has reduced incidence – but is climbing again due to AIDS and antibiotic resistance
 - NZ: 300 notifications per year: European < Maori < PI < Other
- Clinical:
 - Non-specific fever and weight loss (due to macrophage cytokines), coughing, blood-tinged sputum. If in GI, can present with obstruction
 - Takes 6 weeks to 3 months before Tb sensitivity develops (ie Mantoux positive)
 - Predisposing host factors: malnutrition, alcohol, diabetes, age, immune suppression (diseases or drugs), background population prevalence

- Progression:
 - Primary infection: initial exposure is self-limiting, leading to formation of a solitary granuloma (Ghon focus), often with granulomas along lymphatic drainage and in hilar lymph nodes (Ghon Complex). Lesions usually asymptomatic and undergo fibrosis and calcification
 - Spontaneous recovery: may still have bacilli on board
 - Progressive primary infection: rare, primary lesion erodes into airways or vasculature → airway spread or miliary spread → fulminant bronchopneumonia
 - Post-primary pulmonary Tb: granulomas coalesce → consolidation evident on X-ray → cavity ruptures into a bronchus → productive cough, fever, sweating, haemoptysis
 - Secondary infection: in small percentage of those who had primary infection. Reactivation of latent mycobacteria. Usually in lung apices (higher O₂ tension). Can become progressive. Can have isolated involvement of the intestine or adrenals (→ acute Addison's Disease). Cell mediated immunity or delayed type hypersensitivity contributes to tissue destruction
- Diagnosis:
 - Samples: sputum, bronchial wash, gastric lavage in the morning, bronchoscopy, pleural tap
 - Culture (6 weeks), ZN stain, PCR (not very sensitive or specific for serious disease)
- Treatment:
 - Combinations always required for a long duration
 - Drugs:
 - Isoniazid: best and cheapest. Bacteriocidal. Side effects: rash, *peripheral neuropathy, hepatotoxicity*
 - Rifampicin: Destroys rapidly dividing bacilli quickly (⇒ good for fulminant disease). SE: *enzyme induction, orange secretions, rash, flu like illness, purpura*
 - Pyrazinamide: bacteriocidal, works intra-cellularly (ie bacilli inside macrophages). SE rash, *hepatotoxicity, gout*
 - Ethambutol: SE *optic neuritis*. In kids too young to monitor visual acuity, use streptomycin
 - Regime: 2 months of isoniazid + rifampicin + pyrazinamide + 4 months of just isoniazid and rifampicin
 - Compliance a major issue (→ directly observed therapy. Is cost effective compared to self-administered therapy. Treatment completion rates up to 90% are possible), also toxicity
 - May need steroids (in addition to antibiotics) if adrenal suppression, miliary Tb or pleural effusion
- Pathology:
 - Bacterium is ingested by macrophages, but resists lysis due to waxy coat. Multiplies inside macrophage. Immune response forms granuloma through unknown mechanisms
 - Macroscopic appearance: lesions in any organ – but mainly in lungs and lymph nodes. Initially small focus of consolidation < 3cm with central caseation, which cavitates if it communicates with a bronchiole. Resolution → fibrocalcific scarring puckering the pleural surface. Large nodules have extensive cavitation and necrosis, and are lined with a ragged white material containing millions of mycobacteria
 - Microscopic appearance: granulomas composed of epithelioid cells surrounded by fibroblasts and lymphocytes, containing giant cells and Langhans cells (nuclei around the edge). Central caseous necrosis. Acid-fast bacilli with ZN stain

Fungal Pneumonias

- Second most common cause of infectious granulomas
- Often form necrotising granulomas with central cavitation similar to Tb
- Uncommon in NZ: but query in returned travellers or immunosuppressed
- Causative agents:
 - Candida: includes yeast and pseudohyphae. Oral commensal → multiple scattered lesion in the lung
 - Aspergillus: a saprophytic hyaline mould causing bronchopneumonia, possibly with vascular invasion and dissemination → haemorrhage and necrosis. Most common in immunocompromised – especially acute leukaemia
 - Mucormycosis (Zygomycosis): 2 infectious types: Rhizopus and Mucor. Tendency to invade blood vessels and cause haemorrhagic pneumonia
 - Cryptococcus neoformans: pleomorphic round to oval 4 – 10 micron yeast with thick mucinous capsule. Found in bird (pigeon) droppings. Most common infection is meningitis. Stains with Indian Ink stain
 - Others: histoplasma capsulatum, coccidioides immitis and blastomycosis dermatitidis

Viral pneumonias

- Usually acquired through inhalation
- Typically result in diffuse interstitial oedema and lymphocytic cellular infiltrates in the septae. Lungs tend to be heavy and diffusely firm without focal lesions. If severe → microvascular injury → pneumocyte necrosis and leakage of proteinaceous fluid into alveoli → hyaline membrane formation
- Most due to influenza viruses (elderly), respiratory syncytial virus (kids) and rhinovirus (kids)
- Viruses of note:
 - Cytomegalovirus: Herpes virus causing cytomegaly or enlargement of infected cells. May have multiple small cytoplasmic inclusions that are purple and PAS-positive. Subclinical infection unless immunocompromised. Commonest viral pneumonia in immunosuppressed. Focal or diffuse interstitial pneumonia. CMV primarily infects epithelial and endothelial cells
 - Herpes Simplex Virus types I and II. Have characteristic nuclear inclusions in epithelial cells. Two patterns of spread: Necrotising Tracheobronchitis mechanism (spread by contiguity through necrotic mucosa) or Haematogenous dissemination (more random distribution through lung)
 - Varicella Zoster: Lung involvement similar to H. Simplex
 - Measles: RNA virus, infection leads to multinucleate giant cells, interstitial pneumonia, and focal bronchiolar necrosis. Mainly in immunocompromised kids with measles
 - Adenovirus: DNA virus mainly causing mild upper RTI. Clinical disease in transplant patients (eg bone marrow). Necrotising bronchitis and bronchiolitis. Smudge cells seen (large cells with dense mass filling the nucleus)
 - Influenza: RNA virus seen in older adults
 - Respiratory Syncytial Virus: RNA virus causing RTI in the young. Causes bronchiolitis, sometimes necrotising, and less frequently interstitial pneumonia
- Mainly Influenza A or B, Adenovirus or RSV

Other pneumonias

- Mycoplasma pneumonia: Common cause of URTI. Smallest free-living organism. 15% of all pneumonias in general population. Benign and self-limiting with few complications. Peak incidence is 5 – 15 years. Causes a bronchiolar lesion with neutrophil rich exudate, and bronchiolar metaplasia
- Pneumocystis Carinii Pneumonia: Extracellular protozoan parasite almost exclusively infects the lung. Selective attachment to type I pneumocytes → injury. Usually in AIDS. Microscopic appearance: interstitial infiltrate of lymphocytes and plasma cells, and foamy intra-alveolar exudate containing the organism. Stain with silver (GMS). Occurs as cysts, excysted forms and trophozoites. Ground glass appearance on X-ray
- Lipid Pneumonia: Exogenous lipid pneumonia – aspirated mineral oil being taken by the elderly for constipation → segmental opacification (whiting-out) of the lung and granulomatous fibrous reaction. Endogenous lipid pneumonia occurs distal to an obstruction (eg cancer) due to coalescing lipid droplets from dead alveolar macrophages
- Mixed bacterial flora is normally found in patients with chronic pulmonary infections (eg cystic fibrosis, bronchiectasis). Principle organisms are *Pseudomonas Aeruginosa* (commonest), *staphylococcus aureus* and *Haemophilus influenzae*

Community Acquired Pneumonia

Epidemiology

- 1 per 1,000 admitted annually
- Mortality = 10 % (especially old, young, underlying disease)

Pathogens:

	Organism	Proportion	Presentation
Bacteria	Strep. Pneumoniae	60 – 70%	Under 5, Over 50 Abrupt Focal chest signs – usually lobar
	Mycoplasma Pneumoniae	5 – 18%	Kids & young adults, 4 yearly epidemic
	H Influenzae	4 – 5%	Flu like, minimal respiratory signs Type A: Smokers, CORD, all ages, no distinguishing signs Type B in unvaccinated pre-schoolers

	Legionella	2 – 5%	Classic presentation: 40 – 70 year old working smoking man
			Organ transplants
			Fewer respiratory symptoms
			>50% have headache or delirium
			Often diarrhoea/liver pain
			hyponatraemic
	Chlamydia (esp. from farm animals), S	< 3%	
	Aureus, G- anaerobes		
Virus	Influenza	8%	
	Other	2 – 8%	

- Unknown organism in 1/3 of cases despite extensive testing. Dual infections occur
- GI symptoms in typical and atypical
- Clinical clues:
 - 2 – 3 days: pneumococcus, staph aureus
 - 1 – 3 weeks: mycoplasma/legionella
 - Sputum: foul smelling ⇒ anaerobic, rust coloured ⇒ pneumococcal
 - Season: summer ⇒ legionella, mycoplasma comes in 4 yearly cycles
 - Chronic lung disease: H Influenzae, Moraxella catarrhalis (ie β lactams)
 - HIV: PCP
 - Neutropenia: G –ive, fungal
 - Alcohol: G –ive, legionella, staph
- Aspiration (6 – 10%) → ↑risk of anaerobe → cavitation. Upper respiratory commensals
- Cavitation → S Aureus, G- & Tb
- Previous viral infection common in bacteria
- If immunocompromised:
 - Pneumocystis carinii (AIDs)
 - G –ive bacilli: pseudomonas aeruginosa, Klebsiella pneumoniae (neutropenic cancer patients)
 - Fungi: Candida albicans, Cryptococcus neoformans
 - Virus: cytomegalovirus

Diagnosis

- Suggested by fever + respiratory symptoms (cough, sputum, dyspnoea)
- May present with GI symptoms most prominent
- Confused with acute bronchitis
- Signs: fever in > 80%, Respiratory Rate > 20, crackles on auscultation, consolidation in 30%
- Post influenza: 70% (?) S. Aureus infection (→ micro abscesses)
- Can be secondary to abscess, empyema, lung cancer

Investigation Options

- CXR: extent, cavitation, effusion, cardiomegaly. False negatives possible if PCP or during first 24 hours
- Blood gases
- FBC: White cell count, if > 15,000 * 10E9 ⇒ bacteria likely cf. virus
- Urea/electrolytes/liver → severity and underlying disease
- Urine: glycosuria
- Microbiology:
 - Sputum (but 1/3 don't expectorate and many causative organisms are URT commensals): culture and pneumococcal antigen test (most sensitive test for strep pneumoniae). If can't get sputum sample, can nebulise with hypo-osmotic saline.
 - Blood serum for pneumococcal antigen
 - Blood cultures
 - Culture plural effusion
- Lavage via bronchoscopy may be indicated in immunosuppressed patients and in those suspected of TB who can't produce adequate sputum

- Acute and convalescent serum for antibodies to mycoplasma pneumoniae, legionella, chlamydia pneumoniae (Convalescent = 5 – 6 weeks later, a 4 fold rise in antibody titre or the presence of IgM specific antibody is evidence of recent infection)

Prognosis

- Classified as severe if (\uparrow 21 times risk of mortality)
 - Age > 65
 - Respiratory rate > 30 bpm. (*key prognostic indicator*)
 - Systolic BP < 90, Diastolic BP < 60 mmHg or low urine output (ie shocked)
 - Confusion
 - Serum urea > 7 mmol/L
 - Comorbid disease: heart failure, diabetes, CORD, cancer, HIV, renal failure, chronic alcohol, etc
- Other markers of severe prognosis:
 - WBC < 4000 or > 30000
 - PO₂ < 60 or inability to get Sats above 90% despite O₂ therapy
 - CXR shows multilobed or pleural effusion
 - Haematocrit < 30%

Treatment

- Community treatment:
 - Immediate empirical therapy:
 - Should cover S pneumonia
 - Erythromycin if legionella/Mycoplasma suspected
 - Antibiotics: for 5 – 10 days (10 – 14 if Mycoplasma or Chlamydia)
 - Oral amoxycillin 500mg td
 - If allergic to penicillin: erythromycin
 - IV benzyl penicillin 1.2 g qd IV if poor absorption (e.g. vomiting)
 - If severe: erythromycin 1g qd + 3rd generation cephalosporin
 - Types of antibiotics:
 - Penicillin: strep pneumoniae. Even if resistant, iv penicillin dose exceeds the MIC, so it's still effective (doesn't work though for Meningitis caused by Strep Pneumoniae because CSF penetration is lower)
 - Augmentin, Cefaclor, Tetracycline (not kids), cefuroxime (iv): H Influenzae (5% resistant to amoxycillin), Branhamella Catarrhalis
 - Flucloxacillin: Staph aureus
 - Ceftriaxone: penicillin resistant strep pneumoniae, G- bacilli
 - Erythromycin (ie macrolides): mycoplasma, legionella, chlamydia
 - Rifampicin + isoniazid + pyrazinamide: Tb
 - Cotrimoxazole: Pneumocystis carinii
 - Fluconazole or Amphotericin B: Candida, Cryptococcus
 - Ganciclovir: CMV
 - Resistant to Augmentin (ie have β -lactamase):
 - Mycoplasma pneumoniae
 - Chlamydia pneumoniae
 - Legionella
 - Penicillin resistant strep pneumoniae
- Hospital treatment:
 - Only 0.1% of chest infections get to hospital \Rightarrow not typical of population as a whole
 - Hospitalise if high pyrexia, cyanosis, tachycardia, tachypnoea, confusion
 - Oxygen:
 - See Oxygen Therapy, page 60
 - Give sufficient O₂ to keep PO₂ > 60 mmHg
 - O₂ saturation > 90 % preferable
 - Transfer to ICU if:
 - Severe
 - Blood gases bad: PO₂ < 60 on FIO₂ > 60%, or PCO₂ > 48 (should breath faster \rightarrow PCO₂ should fall – if normal or raised person getting tired \rightarrow bad sign)
 - Shocked

- CCHL preferred medicines list:
 - Uncomplicated: Penicillin G 1.2 g iv 4 – 6 hourly or amoxycillin 1g iv 8 hourly. Consider adding erythromycin 500 mg iv 6 hourly if the patient is > 60, no response to penicillin antibiotics, or mycoplasma or legionella are suspected (atypicals less likely if leucocytosis)
 - History of CORD or other disease: Augmentin 1.2 g iv 8 hourly or Ceftriaxone 1.5 g iv 8 hourly. Consider adding erythromycin for above complications

Failure to Respond

- Is treatment failing?
 - Some improvement should be seen in 48 – 72 hours, don't change treatment over this time unless there is a marked deterioration
 - CXR may worsen initially after therapy started: if mild pneumonia this may be normal. If severe, this is a poor prognostic indicator
 - Fever lasts 2 – 4 days, S pneumoniae resolves quickest
 - Crackles will last beyond 7 days in up to 40%. May take more than a month for CXR to clear
- If treatment is failing, consider:
 - Incorrect diagnosis: PE, pulmonary oedema, Wegener's granulomatosis (ie non-infectious illness)
 - Antibiotic resistant organism
 - Resistant infection: mycoplasma, chlamydia, Staph aureus, TB, PCP (immunodeficient)
 - Complication: empyema (see Pleural Disease, page 73), abscess, PE, drug induced fever
 - Underlying disease: lung cause, cardiac failure, immunodeficiency
 - Drug compliance in outpatients

Pleural Disease

- Common problems:
 - Effusion
 - Empyema
 - Pleural pain
 - Pleural disease
 - Pneumothorax. See Tension Pneumothorax, page 490
- Usually presents with pain related to breathing: cough, deep inspiration
- Investigations:
 - CXR: PA, lateral and lateral decubitus (does pleural opacity move with gravity)
 - Pleurocentesis
 - Pleural biopsy
 - US for septa or cysts
 - CT. MRI rarely superior to CT
- Pleural space:
 - Usually 0.4 mls of fluid
 - If ↑ then either ↑ production or ↓ clearance (eg Tb or malignancy blocking lymphatics)
- Pleural fluids:
 - Takes 300 – 500 ml before visible on CXR
 - **Transudate:**
 - Pleural membrane not diseased
 - Due to change in hydrostatic or osmotic pressure due to distant disease
 - Eg nephrotic syndrome, cirrhosis or CHF
 - **Exudate:**
 - Protein rich (> 30 – 40 g/L)
 - Due to pleural disease: Parapneumonic effusion, empyema, malignancy, Tb, SLE/RA, asbestosis, drug induced
 - **Empyema:**
 - = Collection of purulent material (with or without bugs) in any body site: usually refers to pleural space
 - Commonly associated with underlying pulmonary parenchymal infection
 - Low pH differentiates it from effusion, as does growth of organism on culture
 - Strep pneumoniae and Staph aureus are the main pathogens
 - Closely related to lung abscess (necrotising pneumonia)
 - Symptoms: fever, sweats, cough, dyspnoea, weight loss, pleurisy

- Signs: stony dullness to percussion, ↓breath sounds, maybe quite localised, fluid in costophrenic angles on X-ray
- Need to drain. Reduced antibiotic penetration, especially if loculated
- Usually heals with pleural fibrosis
- If blood in a pleural tap then:
 - Hit an artery
 - Haemothorax (need to evacuate. NB can bleed 3 litres into one side of the chest → profound shock)
 - Blood in an effusion (eg Tb/cancer). To differentiate from a haemothorax measure the haematocrit
- Testing pleural fluid:
 - Total protein
 - Albumin: If $(\text{effusion albumin}) / (\text{serum albumin}) > 0.5$ then transudate
 - LDH: ↑ in exudates
 - pH < 7.2 ⇒ empyema
 - Amylase. Normally none. If present then oesophageal rupture or pancreatitis
 - Cytology for malignancy
 - Microscopy and culture: low sensitivity. Organisms causing empyema are hard to culture (eg anaerobes, Tb, fungi, etc)

Venous Thromboembolism

Deep Vein Thrombosis (DVT)

Risk Factors

- Key risk factors:
 - Age
 - Obesity
 - Immobility
 - Co-morbidity
- These can present as:
 - Post-operatively (immobile + hypercoagulable)
 - Stasis (long period of immobility)
 - Pregnancy & immediately post-partum
 - Thrombophilia
 - Smokers on the pill. See Combined Oral Contraceptive, page 341, for risk ratios
 - Obesity, Cancer, Polycythaemia
 - PMHx or FHx of DVT

Presentation

- May be rapidly offset by collateral bypass
- Less than 1/3 present with classic syndrome of calf discomfort, distal oedema, venous distension & pain on forced dorsiflexion of foot
- Homan's sign: pull big toe up → stretch calf → pain. Of little diagnostic value and theoretically could dislodge a clot
- Exclude Baker's cyst: herniation from joint space into popliteal space – wouldn't cause leg swelling
- Approx. 50% are asymptomatic

Investigations

- See Possible Investigations, page 77

Treatment

- Aims:
 - Prevent PE
 - Restore venous patency
- Options:
 - Anticoagulant: See below
 - IV or subcutaneous heparin for 5 days: aim for APTT 1.5 – 2.5 times normal

- Oral warfarin for 3 months: 5mg daily then dose adjust to aim for INR 2.0 – 3.0. Can continue longer – haemorrhages, if they occur, are usually early on
- Surgery: really only if limb at risk. Veins often re-occlude
- Thrombolytic Treatment: better clearance of occlusion, no change to PE risk, ↑risk of bleed or intra-cranial haemorrhage ⇒ little evidence of net benefit
- Prophylaxis:
 - Cost effective if risk high. Base assessment on clinical risk – lab results not good predictor. If low risk after surgery – early ambulation and stockings may be sufficient
 - 2/3rds decrease in risk with Low molecular weight Heparin (inject daily for duration of risk)
 - Mechanical: intermittent external compression with inflatable cuffs as effective as drugs in moderate risk people – but frequently misused
 - Antiplatelet: aspirin not as effective as anticoagulant but good in the community as LMM Heparin not funded (ie can be prescribed by GP for a temporarily bed-bound elderly or obese person)

Anticoagulant Treatment

- **Standard (unfractionated) Heparin:**
 - Potentiates antithrombin III at all sites of coagulation activation (cf Low Molecular weight Heparin which only acts at Factor 10)
 - Dosing:
 - 10 fold variability in individual dose response → individual titration required
 - $T_{1/2} = 100$ minutes
 - Monitor APTT and aim for 1.5 – 2.5. (If goes above 3 then 8 * risk of bleed)
 - Monitor after 10 hours (4 – 5 half lives)
 - Emboli doses:
 - IV dose: Loading 5000 IU, maintenance 1400 IU/j (20 IU/kg/hr)
 - Subcutaneous: 17,5000 IU 12 hourly, duration of action 9 – 10 hours
 - $T_{1/2} \downarrow$ in large PE ⇒ need infusion not bolus
 - Standard Heparin Prophylaxis:
 - Medical view (surgeons disagree!): 5% DVTs in general surgical operations, 20% in orthopaedics
 - Pre-op Prophylaxis:
 - ↓Non-fatal PE by 40% and fatal by 65%
 - ↑Risk of excess bleeding from 3.7% to 6%
 - Low dose heparin (never warfarin):
 - 5000 IU standard heparin 12 hourly start 2 hourly pre-op
 - LMW Heparin single dose: more costly and no advantage in most cases
 - Continue for 2 weeks for patients at high risk (biggest mistake is to stop too soon)
 - Heparin induced bleeding:
 - Uncommon for 1st 2 days, then common for days 3 – 10
 - Retroperitoneal is a common occult site of bleeding
 - Thrombocytopenia after 5 days
 - Antidote: Protamine sulphate + FPP (clotting factors)
- **Low Molecular Weight Heparin:**
 - Lots of different types, all with different $T_{1/2}$ s and doses
 - Longer $T_{1/2}$ (can have once daily dosing), better bioavailability, less platelet inactivation, and potentially less bleeding
 - Elimination is not dose dependent (heparin approaches this at high dose)
 - Need to adjust for obesity
 - Protamine reversal less efficient
- **Warfarin:**
 - Competitive inhibition of Vitamin K dependent clotting factors (II, VII, IX, X) and inhibits proteins C and S
 - Pharmacokinetics:
 - Very narrow therapeutic index
 - 10 fold variability from dose to plasma concentration, and further 10 fold variability from plasma concentration to effect
 - 99% albumin bound ⇒ $V_d =$ intravascular space
 - $T_{1/2} = 25 – 60$ hours, biological effect lasts 2 – 5 days

- Contraindications:
 - Teratogenic, but not in breast milk
 - Risks of bleeding, eg peptic ulcer, haemorrhagic stroke
 - On NSAIDs (\rightarrow GI bleed)
- Consider:
 - Can the patient cope with therapy and monitoring (infirm, alcoholic, etc)
 - \uparrow Warfarin sensitivity if > 65 years due to \downarrow liver metabolism
 - Patient education important – lots of different sized/coloured pills
- Dose:
 - Do pre-test INR
 - Start low, monitor on day 3
 - Dose range approx 3 – 9 mg daily (contrary to New Ethicals)
- Target range for INR:
 - Venous thromboembolism: INR of 2 – 3 for 3 months for 1st VTE
 - Non-rheumatic atrial fibrillation:
 - > 60 with no risk factors: INR 1.5 – 2.7
 - Risk factors: hypertension, previous VTE, recent heart failure
 - Don't anticoagulate patients < 60 years if no risk factors
 - MI: 20% \downarrow in mortality and reinfarction but no advantage of warfarin over aspirin except with added fibrillation (in which case aim for INR 2 – 3)
- Bleeding:
 - Risk factors: age, haemostatic disorder, malignancy, uraemia, GI ulceration, recent surgery, haemorrhagic strokes, low protein states (ie \downarrow clotting factors)
 - Management:
 - If INR < 7 withhold doses until INR in normal range (unless severe bleed)
 - INR > 7 and no prosthetic heart valve: 0.5 mg iv vitamin K (never IM)
 - If INR > 7 and prosthetic heart valve, don't use vitamin K unless evidence of an intercranial haemorrhage
 - If overt bleeding: stop warfarin, give FFP or Prothrombin complex concentrates
- Drug interactions:
 - Inducers: take 10 days to \downarrow warfarin concentration, and warfarin toxicity when stopped. Phenytoin, carbamazepine, phenobarbitone, rifampicin
 - Inhibitors: immediate effect \rightarrow warfarin toxicity. \downarrow INR when these are stopped: macrolides, metronidazole, fluoxetine, quinolones (eg ciprofloxacin), chloramphenicol, cimitidine, disulphiram
- If massive PE, consider thrombolysis. Echocardiogram to determine RV function useful in assessing risks and benefits

Pulmonary Embolism (PE)

- Very important to do a risk assessment for *everyone* in hospital or bed-bound at home: are they low, medium or high risk. Prevention is better than cure

Presentation

- Frequently undiagnosed (71% of PEs are not diagnosed): *always have it as a differential to SOB*
- If episodic SOB unresponsive to treatment \rightarrow ?PE
- May not have chest pain. May have fever, but rarely sweating or rigours
- Severity:
 - Small: transient chest pain, cough, SOB. If pre-existing pulmonary disease may get small infarct with pleuretic chest pain and fever
 - Multiple small emboli: pleuretic chest pain, haemoptysis, gradually \uparrow SOB
 - Medium: Bronchial arteries are enough to maintain viability of healthy lung tissue. Get chest pain (not always pleuretic), SOB, maybe haemoptysis
 - Large: Classical – 10 days post op, sudden SOB and collapse while straining on toilet. If fatal, die within an hour. May mimic MI with comma (acute SOB, severe chest pain, hypotension, temp, \uparrow LDH, syncope). Also cyanosis, gallop rhythm, \uparrow JVP, pleural rub, haemoptysis
- Course: Frequent PE \rightarrow pulmonary hypertension \rightarrow dilated pulmonary artery \rightarrow enlarged right heart (Cor Pulmonale)

Possible Investigations

- Imaging:
 - CXR: most are normal
 - Doppler US for DVT
 - Ventilation-Perfusion Scan
 - Pulmonary arteriogram: gold standard but not often done
 - CT Pulmonary Angiogram: pretty good and getting better
- ECG:
 - Small-medium PE: usually normal except for tachycardia. May be signs of AF or right ventricular strain
 - Massive PE: S1Q3T3 pattern: S wave in lead I, Q wave in lead III, inverted T wave in lead III. Tall peaked T waves in lead II.
- Bloods:
 - ABGs: Aa gradient
 - FBC - check Hb, WBCs, platelets (eg ↑ → hypercoagulable)
 - Clotting times: likely to be normal – these test bleeding disorders, not clotting disorders
- D-dimmer test for fibrin degradation products → digested clot (cheap and easy):
 - +ive for cancer, trauma, post surgery, sepsis → lots of false positives
 - Don't use as first line test – only in the context of a complete algorithm
- Decision analysis:
 - If > 6% risk of a PE then test
 - If > 48% risk of a PE then treat
 - If risk > 6% but < 48% then further testing
 - Test sequence:
 - Chest X-ray and D-dimmer: if d-dimmer negative then no DVT/PE. Positive test doesn't change pre-test odds. If Chest X-ray normal then V/Q scan. If abnormal go straight to CT angiogram
 - V/Q Scan: if positive then treat. If negative, doesn't change pre-test odds
 - CT angiogram

Treatment

- See Anticoagulant Treatment, page 75
- If massive (Hypotension and multiple clots): thrombolysis or surgery
- If submassive (RV strain or lots of clots): consider thrombolysis

Asthma

- Is chronic and obstructive, but not usually categorised with CORD

History

- Viral infections likely to trigger asthma
- Night time cough and low peak flow can be asthma, ?hay-fever, a cold or bronchitis
- Ask about:
 - Living situation
 - Occupation
 - Allergies, any pets?
 - Seasonal
 - Cold air
 - Irritants (eg fumes)
 - Exercise
 - Night cough
 - History of atopy: eczema
- Classic symptoms: SOB, wheeze, cough, tightness (like in angina)

Assessment

- *Always do peak flow.* Not the same as FEV1, which is more accurate. FEV1 of 50% of predicted = PF of 70% predicted
- If can't get a wheeze on auscultation, then take a big breath and blow out fast to elicit wheeze (=Forced End Expiratory Wheeze). Also listen to heart to ensure it's not a cardiac cause

- Can you demonstrate reversible bronchial constriction? If peak flow (or FEV1 if spirometry available) ↑ by 15% (60 – 70 litre/min) following bronchodilator. Do best of 3 peak flows, then repeat 15 minutes (= peak response time) after >= 2 doses of a reliever
- There will be significant pathology even if mild: pseudo stratified epithelium gone, thickened basement membrane, ↑eosinophils, hypertrophy of smooth muscle and glands, ↑mucus
- High-risk asthmatic (markers of ↑ risk of death):
 - Hospital admission in last 12 months
 - Previous life threatening attack
 - Repeated self-administration of high doses of reliever (eg requesting 2 or more reliever prescriptions per month)
- Precipitating factors in a life-threatening attack:
 - In kids (80%) and adults (30%): viral URTI. Most commonly rhinoviruses and coronaviruses ('common cold')
 - Allergen exposure in a sensitised individual
 - Drug sensitivity, eg aspirin
- If severe, then ?other causes: PE, pneumothorax, etc

Classification of severity

- How they feel (ie breathlessness) does NOT correlate to severity (as measured by FEV1). Due to temporal adaptation – if chronically breathless, body turns off perception of breathlessness (cf don't hear trains if living by a railway line). Unless you MEASURE lung function, you CANNOT assess severity. However, in kids have to rely on symptoms as peak flow unreliable

	PEF	Symptoms	Action
Under Control – stable	> 80% predicted (best PEF they've ever had)	Can exercise easily, symptom-free most days, Not needing reliever on most days.	Take preventer every day – can it be reduced? Would a spacer help?
Getting Worse - unstable	< 80%	Daily symptoms, waking at night, getting a cold, more short of breath with exercise, needing more reliever	Start or increase dose of preventer. Use reliever as required.
Severe	< 60%	More breathless or wheezy, reliever only lasting 2 – 3 hours. Getting worse despite more preventer	Start prednisone and see doctor within 1 or 2 days. Use reliever as required.
Emergency	< 40%	Hard to speak, feeling faint or frightened, reliever not working.	Ambulance/emergency doctor, sit upright, keep calm, keep using reliever.

- Key time to measure peak flow is when asthma is getting worse. No one will do it all the time so don't ask them to

Asthma in Young Children

- See Asthma in Young Children, page 613

Principles of management

- Asthma self-management plans are recommended as essential in the long-term treatment of adult asthma. Those with formal management plans have half the morbidity of those without them, despite the same treatment
- Also need to establish, avoid and control triggers
- Factors associated with asthma deaths:
 - Long term:
 - Lack of appreciation of chronic asthma severity and risk
 - Poor compliance
 - Discontinuity of medical care
 - Under utilisation of inhaled steroids
 - Fatal attack:

- Delay in seeking medical help
- Inability to recognise severity
- Over-reliance on bronchodilator
- Insufficient systemic steroid use
- Lack of written information
- If the management plan is too complicated for the patient, modify (eg just the point at which to see the doctor)
- Compliance is critical ⇒ ownership of treatment by the patient is fundamental – negotiate and educate

Treatment

- Status asthmaticus: severe acute asthma that does not respond to treatment. See Asthma, page 485
- Most important part is use of inhaled corticosteroid. Patient may favour reliever (it obviously does something – reinforce that preventer stops it happening to start with)
- Inhaled Corticosteroids:
 - Action: Anti-inflammatory and ↓hyper-reactivity
 - Effect: ↑lung function, ↓symptoms, ↓admissions (only drug to do this)
 - If using a β-agonist most days then should be on an inhaled steroid
 - Doses:
 - 200 to 1000 µg/day of Beclomethasone Dipropionate (BDP/Becotide) or Budesonide (BUD/Pulmicort), or
 - 100 to 500 µg/day of Fluticasone Propionate (Flexatide - only difference is potency, not efficacy, ?↓side effects)
 - Starting dose: if steroid naïve, better to start low and step up not start high and step down – too hard to wind it back
 - Back titration: in stable patients back titration may be attempted. ½ dose as a one off. If cut too far too fast can rebound within a month. Stopping treatment altogether is likely to cause a relapse
 - Doses by severity:
 - Stable: inhaled steroid bd, β agonist prn. If well controlled can take total steroid dose once a day at night rather than bd → better compliance
 - Unstable: inhaled steroid qid, β agonist prn. If still not controlled then oral theophylline at night or long acting β agonist
 - Severe: systemic steroids, high dose β agonist, O₂, medical review. Bronchodilators and inhaled steroids don't work so well in severe asthma as the major cause of obstruction is mucus plugging and the drugs don't get through. Steroid dose: start early (takes approx 12 hours to have an effect), 0.4 – 0.6 mg/kg/day = 40 mg for normal adult. In practice: 30 – 40 mg/day until PEF normal, then 20 mg/day for as many days again
 - Side-effects: Dose dependent redistribution of fat, electrolyte disturbances, hypertension (ie Cushing's features), stunted growth in children
- Bronchodilator:
 - Reliever. Short acting inhaled β agonist.
 - Potent and rapid bronchodilator and a relatively low toxicity. Relaxes airway smooth muscles (plus other effects, e.g. ↓release of mast cell mediators). Adverse effects: muscle tremour and tachycardia common. Use as needed – not regularly – then becomes a guide to severity
 - Salbutamol and terbutaline sulphate common.
 - Long acting agonists for more severe asthmatics: Salmeterol and Eformoterol (similar effect but ↑ potency). Peak effect 2 – 4 hours, duration 9 – 12 hours.
 - Theophylline:
 - May have additive effect with β agonist, but ↑risk of side effects (including ↓K).
 - Narrow TI.
 - ↑T½ in heart and liver failure, viral infections, elderly, enzyme inhibitors eg: cimetidine, erythromycin, contraceptives
 - ↓T½ in smokers, chronic alcohol, phenytoin, carbamazepine, rifampicin, and barbiturates
 - Given IV (very slowly) as aminophylline (too irritant for IM) for severe attack unresponsive to nebuliser
- Others:
 - Sodium cromoglicate: non-steroidal preventer – less effective than steroids but fewer side effects. Single dose good for prevention of exercise induced asthma

- Anti-leukotrienes: Leukotrienes → ↑vascular permeability, ↑mucus production, ↓mucus transport, etc. Oral montelukast → 15 % ↑ in FEV1, ↓use of β agonist. Place in therapy still uncertain
- Follow-up (eg good liaison with GP) following emergency admission is critical to preventing recurrence

Inhalers

- Advantages: minimum possible dose, highly targeted, patient controls therapy
- Inhaled steroids → deposition in mouth. If not using spacer, need to rinse, gargle and spit otherwise risk of thrush and croaky voice. At best, 10% gets to lower airways without spacer
- Metered dose inhalers (MDI):
 - Autohaler: shake, push lever up, suck. Lower level of suck needed than powder inhalers – but still require good suck to get lower airways deposition. As expensive as powder inhalers. OK from age 8 upwards
 - Standard MDI: (cheap, light and rapid delivery of drug, but co-ordination difficult). From age 12 onwards. Instructions for use:
 - Shake an inhaler between each puff
 - Remove cap
 - Hold it upright and pointed backwards
 - Breath out
 - Fire during 1st 25% of long slow inhalation
 - Hold breath
 - Breath out after removing inhaler from mouth
- Inhalers through a spacer:
 - As effective as a nebuliser. Increases LRT deposition by 4 times
 - Eliminate oral deposition of steroids and ↑ lung deposition of both preventers and relievers
 - Breath-a-tech with a facemask up to 6. Remove mask as soon as you can (stops nasal filtering – try at age 4 - 5). Need smaller spacer as they have a small tidal volume
 - Volumatic without facemask. Need to be able to mouth breath well (ie try from age 2 – 3 onwards)
 - Need to inhale within 30 seconds of a puff into the space
 - One puff at a time
 - But plastic spacer → static charge → particles stick. So wash in detergent once a week and do not rinse bubbles off (→ microfilm of detergent)
 - If using a new space without washing, need to prime it (10 puffs). Don't do this in front of patient
- Dry Powder Inhalers: ↑↑ oral deposition. Use from age 5 up (good for use at school when they don't want to lug a spacer around but their MDI technique is inadequate). Advantages: light, quick delivery, don't need co-ordination, CFC free. Disadvantages: cost, require high respiratory flow
 - Accuhaler: 60 doses, easy to use, has dose meter
 - Disk haler: 6 doses
 - Turbohaler: easier to use than disk haler. Red mark inside indicates when its empty

Chronic Obstructive Pulmonary Disease (COPD)

- = Increase resistance to air flow due to partial or complete obstruction at any level
- = Permanent or minimally reversible obstruction of expiratory airflow caused by chronic bronchitis, emphysema or both
- Lung Function results:
 - FEV1/FVC ratio < 70% with a concave expiratory loop
 - ↑RV secondary to air trapping
 - ↓DL CO due to loss of parenchyma
 - Severity:
 - Mild: FEV1 > 50% predicted
 - Moderate: FEV1 35 – 49% predicted
 - Severe: FEV1 < 35% predicted
- Chest Xray:
 - Emphysema: absent peripheral vessels, hypertranslucency, flattened diaphragm, bullous change
 - Bronchitis: thickened bronchial walls (especially end on)

- Abnormalities in gas exchange:

	Pink Puffer (Emphysema)	Blue Bloater (Bronchitis)
Presentation	Dyspnoea	Cough, sputum, RHF
CXR	Hyperinflated	↑markings at bases
ABG	↓PaO ₂ , ↓PCO ₂	↓↓PO ₂ , ↑PaCO ₂
Lung Function Tests	↑TLC, ↓DL CO	Normal TLC and DL CO
Sleep	Moderate desaturation	Marked desaturation

- Treatment:
 - Only smoking cessation and long term oxygen alters the natural course
 - No evidence that daily bronchodilators are beneficial in asymptomatic patients
 - 20% benefit from oral corticosteroids. Should be used primarily for exacerbations. Inhaled steroids show no significant benefit
- Management of an exacerbation:
 - Exclude differentials: PE, LVF, pneumothorax, hyperventilation
 - Is there an infective component: Upper or Lower RTI
 - Are there complications of COPD:
 - Cor pulmonale/pulmonary hypertension (look for signs of RH failure)
 - Polycythaemia secondary to chronic hypoxia
 - Low body weight/osteoporosis (from steroids and acidosis)
 - Investigations:
 - FBC (is Hb or WBC ↑), U & E, Glucose
 - ECG
 - If Sats < 92% then ABG
 - CXR
 - Sputum microscopy, culture and sensitivity
 - Peak flow is asthmatic component
 - Spirometry when resolved
 - Echo if cor pulmonale or LVF suspected
 - Treatment:
 - O₂ with goal of saturation 90 – 92% (beware CO₂ narcosis)
 - Broncho dilation: Combivent
 - Antibiotics: Usually oral. Augmentin, erythromycin, etc. Commonly H Influenzae or M Catarrhalis
 - Steroids: 30 – 40 mg/day, stepping down over around 2 weeks

Chronic Bronchitis

- = Persistent cough with sputum for at least 3 months in 2 consecutive years
- Follows prolonged exposure of the tracheobronchial trees to non-specific irritants → hypersecretion of mucus and structural changes
- Types:
 - Simple chronic bronchitis: no airway obstruction
 - Chronic asthmatic bronchitis: intermittent bronchospasm and wheezing
 - Chronic obstructive bronchitis: heavy smokers with chronic airways obstruction, usually with emphysema. *Sputum will be clear/white*, only occasionally will be infected (yellow/green)
 - [Cf Chronic infective bronchitis with green sputum ⇒ bronchiectasis]
- Pathogenesis:
 - Chronic irritation (eg inhaled substances such as smoking) and microbiological infections → hyper-secretion of mucus obstructing airways. Hypertrophy of submucosal glands in larger bronchi and hyperplasia of goblet cells in small airways.
 - Infection maintains the hyper-secretion and causes acute exacerbations
- Macroscopic appearance: hyperaemia, swelling, mucopurulent secretions in the bronchi
- Microscopic appearance: increased size of mucous glands. Reid index (ratio of mucous gland layer to thickness of epithelium to cartilage) greater than 0.4. Chronic inflammation → metaplasia to squamous epithelium and dysplasia. Mucous plugging, inflammation and fibrosis. If severe → luminal obliteration

Emphysema

- Enlargement of air-spaces distal to terminal bronchioles and destruction of alveolar walls without fibrosis

- Moderate to severe emphysema is rare in non-smokers
- Aetiology:
 - Cigarettes: usually had a 20-pack year history. Only 15 – 20% of smokers develop obstruction
 - Alpha-1 antitrypsin deficiency
 - Dusts: coal, gold mining, textile, cement and steel making
- FEV1 best single indicator of prognosis
- Pathogenesis: Disruption in balance of elastin synthesis: ↑ in elastolytic activity from neutrophil elastase (smoking → ↑neutrophils) and ↓α1-antitrypsin (elastase inhibitor – oxidants in cigarette smoke inhibit α1-antitrypsin). Neutrophils also release free radicals that inhibit α1-antitrypsin
- Types:
 - Centriacinar (Centrilobular): enlargement of respiratory bronchioles, distal alveoli are spared. (Small particles deposited here – don't make it right to the end). More severe in upper lobes. Blackened. Bronchi and bronchioles have chronic inflammation. Seen in smokers and coal workers pneumoconiosis
 - Panacinar (Panlobular): acinus is uniformly involved from respiratory bronchiole to terminal alveoli. Seen in α1-antitrypsin deficiency (ZZ or MZ alleles on chromosome 14) and as an extension of centrilobular emphysema in smokers. Mean age of onset is 45 – 50 years in non-smokers and 30 – 40 in smokers. Liver disease in 5 – 10 % of adults. Heterozygotes (MZ) predisposed to emphysema if they smoke. Treatment same as for smoking induced
 - Paraseptal (distal acinar): proximal acinus is normal, distal part affected. Most prominent sub-pleurally and next to interlobular septi. Often seen in cases of spontaneous pneumothorax in young people
 - Irregular emphysema: acinus irregularly involved. Associated with scarring
- Macroscopic appearance: voluminous lungs
- Microscopic appearance: large abnormal airspaces, blebs and bullae. Bronchitis and bronchiolitis
- Clinical features:
 - 60 years or older
 - Prolonged history of exertional dyspnoea
 - Minimal non-productive cough
 - Usually have lost weight
 - Use accessory muscles for respiration
 - Prolonged expiration period (lungs collapse due to ↓elastin)
 - Pink puffers: ↑respiratory rate maintains O₂. Xray: ↑central pulmonary artery size, ↓peripheral vascular markings
 - Blue bloaters: ↑PaCO₂, ↓PaO₂, cyanotic, respiratory centre insensitive to CO₂, instead rely on hypoxic drive to breathe. Dangerous to give O₂ → ↓ventilatory drive
- Medical management:
 - Bronchodilators and inhaled corticosteroids: only if reversible obstruction
 - Smoking cessation (nicotine replacement doubles quit rate)
 - Antibiotics
 - O₂ with care
 - Exercise/physio
 - Attention to nutrition

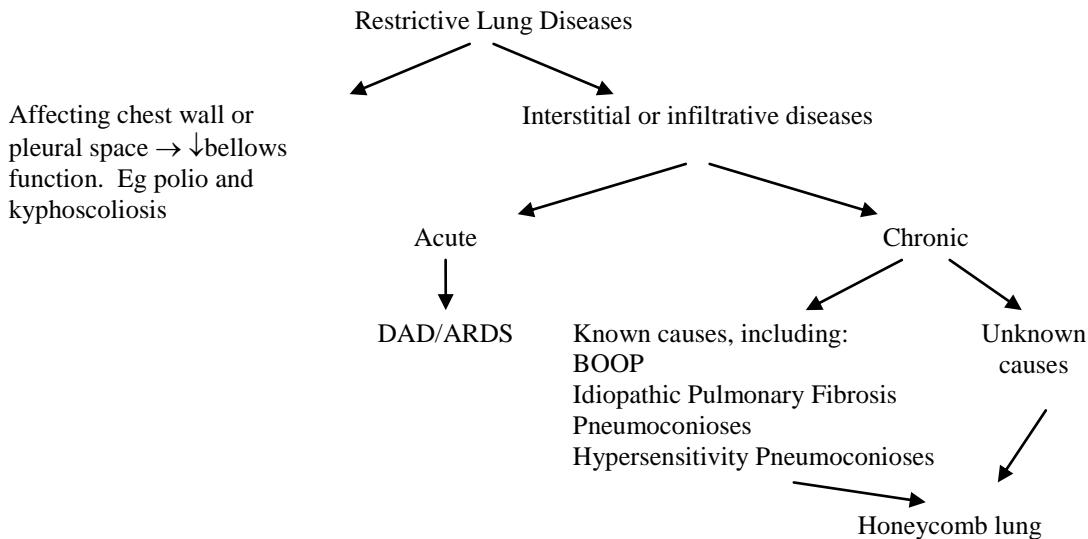
Bronchiectasis

- Chronic necrotising infection of bronchi and bronchioles (ie *a pneumonia that doesn't clear*) → abnormal airway dilation and destruction of bronchial walls → obstruction due to inflammation, ulceration and distortion
- = Chronic infective bronchitis
- Pathogenesis:
 - Obstruction (especially during growth) due to tumour, foreign bodies, mucous impaction (eg in cystic fibrosis and immotile cilia)
 - Infection with bronchial wall weakening and atelectasis (eg in necrotising pneumonia). Especially Tb, pertussis, MAC
- Macroscopic appearance: affects lower lobes, especially vertical airways and more distal bronchi. Airways may be cylindrical, fusiform or saccular
- Microscopic appearance: Acute – inflammatory exudate with desquamation and ulceration of the epithelium. Chronic – peribronchial fibrosis

- Clinical course: foul, bloody sputum, especially in the morning. (cf *Clear sputum in chronic bronchitis*). Repeated ‘bronchitis’ with wheezing, haemoptysis, and dyspnoea. Coarse crepitations, wheezing, and clubbing.
- Complications: obstructive ventilatory insufficiency → dyspnoea and cyanosis. Rarely cor pulmonale, metastatic brain abscesses and amyloidosis

Restrictive/Interstitial Pulmonary Disease

- = Reduced expansion of the lung parenchyma
- British and Americans give them different names
- Over 150 different disease processes primarily affecting alveoli epithelium, interstitium and capillary endothelium, not airways



- Leads to ↓expansion of lung parenchyma, ↓total lung capacity, ↓lung compliance
- Other causes:
 - Secondary to drugs (eg amiodarone)
 - Secondary to radiotherapy
 - In some connective tissue diseases (eg Ankylosing Spondylitis)

Acute Interstitial Lung Disease

Adult Respiratory Distress Syndrome (ARDS)

- = Diffuse Alveolar Damage (DAD)
- = Shock Lung
- Clinical: rapid onset of life-threatening respiratory insufficiency, cyanosis and hypoxaemia refractory to O₂ therapy
- Diagnostic criteria: acute onset, fluid on CXR, capillary wedge pressure < 19 (⇒ not LH failure), hypoxia
- Aetiology – types of injury:
 - Aspiration: gastric contents or drowning
 - Inhalation of fumes or toxic aerosols, smoke, chlorine, oxygen toxicity
 - Circulating toxins: bacterial endotoxins
 - Other: DIC, high altitude, trauma, radiation therapy, chemotherapy
- Pathogenesis:
 - Results from leakage from capillaries to alveoli spaces: non-cardiogenic pulmonary oedema
 - Leads to a non-compliant lung: smaller tidal volume, poor gas exchange, ↑risk of lung rupture when ventilating
 - Prototypical injury is oxygen toxicity: hyperoxia damage alveolar macrophages (AM) → release O₂ radicals → injure lung tissue; AM release cytokines → attract neutrophils, stimulate intravascular adherence, and release further O₂ radicals. Vicious circle of damage, especially to septum
 - Other possible initiating mechanisms (alone or in combination): activation of complement cascade, neutrophil aggregation, activation of coagulation → fibrin deposition, etc

- Macroscopic appearance: Affects WHOLE lung (if only one lobe affected ?pneumonia). Heavy lungs due to fluid accumulation (interstitial and later alveolar)
- Microscopic appearance:
 - Early change: interstitial oedema, few cell infiltrates
 - Acute exudative stage: microvascular injury → breakdown of basement membrane → leakage of plasma proteins into alveoli. Sloughing of injured type 1 pneumocytes. Cell debris + exudate form hyaline membrane. Inflammatory cells in interstitium. No neutrophils in alveoli (key differential from pneumonia)
 - Proliferative stage: Type II pneumocytes proliferate to cover alveolar surface. Fibroblasts lay down collagen in interstitium and alveolar spaces → interstitial and intra-alveolar fibrosis
- Prognosis: 50% mortality. Surviving patients may have mild to extensive diffuse interstitial pulmonary fibrosis

Acute Interstitial Pneumonia (AIP)

- = Hamman-Rich Disease
- Rapidly progressive interstitial pneumonitis that resembles the organising stage of DAD (?may be a variant)
- Affects young adults, presenting with flu-like syndrome and bilateral infiltrates. Most die of respiratory failure within two months

Chronic Infiltrative (Restrictive) Lung Disease

- Common clinical and radiologic features but diverse aetiology and pathology
- Clinical features:
 - Cyanosis due to severe hypoxemia from ventilation-perfusion mismatch
 - Clubbing of digits
 - Late in disease: pulmonary hypertension due to destruction of alveolar capillary bed
 - Interstitial infiltrate and some exudate in small airspaces
- Diseases leading to chronic infiltrative lung disease:
 - Idiopathic chronic interstitial pneumonias: 13%
 - Environmental lung disease: 25%
 - Sarcoidosis: 20%

Types of Idiopathic Pulmonary Fibrosis (IPF)

- Usual Interstitial Pneumonia (UIP, US):
 - = Cryptogenic Fibrosing Alveolitis (UK)
 - Most common type of IPF
 - Presents with gradual onset of dyspnoea and cough (usually dry)
 - Non-uniform slowly progressive disease starting in middle age. Die in several years. No known treatment (don't respond to steroids). Airflow and blood flow disrupted
 - Macroscopic appearance: when advanced lung is small and firm with a honeycomb appearance on cut section
 - Microscopic appearance: ranges from normal to fibrotic alveolar walls, with marked variation in the degree of fibrosis from field to field (cf other IPFs which are uniform). Capillary bed slowly destroyed → pulmonary hypertension and cor pulmonale. Inflammatory cells (lymphocytes + macrophages + neutrophils) in interstitium and airspaces
- Desquamative Interstitial Pneumonia (DIP): more uniform than UIP, with no alternating areas of scarring and normal lung. Filling of alveolar with alveolar macrophages (not desquamated as originally thought). Is it an early stage of UIP? However, may respond to steroids and have a better prognosis. X-ray shows bilateral lower lobe ground glass infiltrates
- Lymphocytic Interstitial Pneumonia (LIP)
- Granulomatous Interstitial Pneumonia

Bronchiolitis Obliterans Organising Pneumonia (BOOP)

- Obliterans ⇒ airways sealed off
- Organising ⇒ fibrosis
- Common response to lung injury from infections, inhaled toxins, drugs, etc
- Major finding: plugs of loose fibrous tissue filling bronchioles and alveoli. Variable chronic inflammatory cell infiltrate is present
- Patients improve gradually with steroids (ie different from UIP)

Pneumoconioses

- = Pulmonary diseases caused by the inhalation of inorganic dust (usually stimulating fibrosis)
- **Asbestos:**
 - Occupational exposure to asbestos is linked to:
 - Localised fibrous plaques: dense fibrotic plaques on X-ray – generally asymptomatic
 - Pleural effusions → cough, SOB
 - Asbestosis: Parenchymal interstitial fibrosis. Progressive SOB on exertion. ↓FVC, ↓FEV but ↑FEV/FVC, ↓DL CO, restrictive pattern
 - Bronchogenic carcinoma (5 times risk, 14 times risk if smoker): most common
 - Mesotheliomas (1000 times risk) but still rare. See Types of Lung Cancer, page 88
 - Laryngeal and perhaps extrapulmonary neoplasms
 - When asking about occupational exposure, need to go back a long time. Will present in an older man. Ask them what they did when they left school and go from there.
 - Pathogenesis: depends on which type of asbestos. Serpentine crysotile form (curly, flexible) is more common, less dangerous, cleared more easily from bronchi and more soluble so don't persist in the alveoli. Amphibole type (straight, stiff, brittle) rarer, more dangerous, go deeper, penetrate epithelial cells and lodge in the interstitium
- Coal Workers Pneumoconiosis (CWP):
 - Two forms:
 - Simple CWP: accumulation of dust laden macrophages with little pulmonary dysfunction
 - Complicated CWP: progressive fibrosis induced by macrophages
 - Macroscopic appearance: Anthracosis, coal nodules progressing to black scars larger than 2 cm in complicated CWP
 - Microscopic appearance: Coal laden macrophages, fibrous scarring
 - Caplan's Syndrome: Rheumatoid arthritis with a pneumoconiosis → nodular pulmonary lesions
- Silicosis:
 - Exposure to crystalline silicon dioxide: sand blasting, rock mining, foundry work
 - Silica causes activation and release of inflammatory factors by macrophages
 - Morphology: discrete pale to black tiny nodules which coalesce into fibrous scars

Hypersensitivity Pneumonia

- = Extrinsic Allergic Alveolitis
- Sometimes grouped with Pneumoconioses → Occupational Lung Disease
- Immune resistance to protein antigens → acute or chronic attacks on re-exposure
- Lots of causes: farmer's lung (antigen is thermophilic actinomycetes), pigeon breeder HSP, air-conditioner HSP
- Morphology: chronic inflammatory cells in the alveolar septi, septal fibrosis, obliterative bronchiolitis and non-necrotising granuloma formation (diagnostic on biopsy)

Honey Comb Lung

- End stage of many chronic interstitial lung diseases
- Morphology: small lungs with nodular pleural surface due to interstitial fibrosis retracting the pleura. Large air spaces cause honeycomb effect. Destruction of the capillary bed in the lung → pulmonary hypertension, RV hypertrophy, cor pulmonale → death

Sarcoidosis

- Multisystem disorder, most common in the young and in females
- Aetiology: ?antigenic stimulus → cell mediated (type 4) immune injury
- Pathogenesis: poorly understood. Deficient cell mediated immunity. Eg anergic to the TB skin test. Stimulated B-cell population with resultant hyperglobulinaemia. ?Antigen → T cells inducing B cells. Monocytes recruited → granuloma formation
- Macroscopic appearance: Chest X-ray shows bilateral hilar lymphadenopathy and/or diffuse interstitial disease. Granulomas also found in spleen, liver, bone marrow, skin, eye and salivary glands
- Microscopic appearance: non-caseating (non-necrotic) granulomas (unlike TB). Occur in all organs but most commonly in all parts of the lungs. Tightly clustered epithelioid histiocytes, multiple giant cells, and a few peripheral lymphocytes
- Clinical course: Treat with steroids. 70% recover, 20% have some loss of function, 10% die

Neoplasia of the Respiratory Tract

Cancer of the Nasal Cavity and Paranasal Sinuses

- Inflammatory Polyp:
 - Not a true tumour: overgrowth of stromal tissue – no malignant potential
 - Common in adults, rare in children
 - Associated with cystic fibrosis
- Sinonasal papilloma:
 - Benign. Can become malignant. 3% become malignant after removal (poor prognosis). 3% have malignancy in polyp (prognosis better)
 - Usually in adult. Presents with nasal obstruction and painless epistaxis
 - ?Associated with HPV 6 & 11
- Sinonasal Carcinoma:
 - Occupational association: wood turners (adenocarcinoma) and nickel mining
 - Relatively rare (<1% of cancer deaths)
 - 60% 5 year survival, surgical treatment
 - Squamous cell most common (look for keratin whorls), also adenocarcinoma
 - Stromal overgrowth = desmoplasia ⇒ sign of invasive cancer
- Nasopharyngeal Carcinoma:
 - Most common in SE Asia and N Africa, occurs in 15 – 25 and 60 – 69. Presents with epistaxis or obstructed eustachian
 - No occupational association
 - Associated with EBV
 - Biphasic tumour: Small cells superimposed on squamous cell carcinoma, with lots of lymphocytes (don't confuse with lymphoma)
 - Aggressive: early lymph node spread
 - Treatment: radiotherapy +/- surgery

Tumours of the Larynx

- Benign non-neoplastic neck lumps:
 - Inflammatory:
 - Lymph nodes: anterior cervical for tonsillitis, jugular digastric for tongue
 - Atypical Tb (especially kids)
 - Deep Neck abscesses: para-pharyngeal or retro-pharyngeal abscesses (can track down into mediastinum)
 - Thyroglossal cysts: cysts in embryological track from tongue to thyroid (usually at level of hyoid)
 - Branchial cysts: ?embryological. Like enlarged anterior node. Contain lots of cholesterol
 - Pharyngeal pouch: Mucosa herniates out through triangle between the cricopharyngeus and thyropharyngeal muscles under pressure from swallowing when upper oesophageal sphincter doesn't relax properly. Catches food, becomes infected. Treatment: surgery
- Laryngeal Nodule:
 - Due to trauma of vocal chords banging together → oedema (early) → scarring/granulation tissue (late)
 - Only on anterior 1/3rd of vocal fold
 - Completely benign
 - Gravely voice
- Laryngeal Papilloma:
 - Like sinonasal papillomas
 - Most commonly seen in children
 - Associated with HPV 6, 11
 - Tendency to recur: can become unmanageable → airway obstruction
 - Benign → squamous overgrowth
- Laryngeal Carcinoma:
 - Presentation:
 - Presenting early: if affect vocal chords, invade recurrent pharyngeal nerve, front of mouth
 - Presenting late: supraglottic lesions due to airway obstruction or pain (⇒ deeper), sinus (lots of space)
 - Dysphagia rare

- 90% are squamous cell carcinoma (like lung)
- Mostly in males, smoking a major risk factor, also alcohol, radiation, family history, tend to be older (> 50)
- Classification, prognosis and treatment depends on site (prognosis also depends on stage):
 - Glottic: 60%, on chords, maintained in larynx by cartilage. Treatment: radiotherapy unless spread through cartilage
 - Supraglottic: 30%, above chords, involves false chord. More aggressive, metastasise to cervical lymph nodes
 - Transglottic: < 5%, crosses from one chord to another
 - Infraglottic < 5%, below chords, more aggressive
- Don't usually metastasise elsewhere, but lymph node infiltration common
- Treatment: radiotherapy (→ dry mouth) +/- surgery (superficial, hemilaryngectomy, laryngectomy, laryngectomy +/- radical neck resection. Chemo has little effect against SCC (most of them). If laryngectomy then need a tracheostomy (→ can't cough, ↑infection, ↓humidification, etc)

Lung Cancer

Smoking

- 1998 Statistics for NZ:

Adults	24%
Male	25%
Female	23%
Maori	44%
Maori Male	40%
Maori Female	47%

- Cigarette smoking and lung cancer:
 - Relative risk is 10 times in regular smoker, 20 times in those smoking > 40 per day
 - Most important avoidable cause in 20 – 30% of cancers: including Respiratory tract, liver, stomach, cervix
 - Tobacco and alcohol have a multiplicative relationship in oral cavity, throat and oesophagus
 - Fall in lung cancer mortality begins 5 – 9 years after quitting, back to baseline at 14 years
 - Abnormal cytology and squamous metaplasia in smokers
- Passive smoking:
 - Passive smoking: relative risk is 3 times normal
 - Relationship to URTI in children
 - Possibility of younger children being affected e.g. SIDS
 - Children of smokers more likely to smoke
- Active Smoking:
 - Demonstrates that knowledge/education is insufficient to ensure behaviour or behaviour change
 - Health promotion principles of acting at all levels (i.e. individual/community/government) to make healthy behaviour the easy choice
- Measurement: Pack-years = (cigarettes per day * years smoked) / 20
- Smoking cessation:
 - Listen first: Why do you smoke? (If it's stress – what will you do in the future)
 - What do you know about risks (don't assume they know about risks – maybe information lack or cognitive dissonance)
 - Estimate cost for them: what would you do with \$2-3,000 per year
 - Give a positive message: do you want to live longer/better
 - Need to negotiate with patient: be smart not paternalistic, be realistic, honest
 - Always put smoking on problem list
 - Information: Quit Book or Can Quit (from cancer society). Quitline 0800 778 778

Epidemiology of Lung Cancer

- Commonest cancer in the world
- In New Zealand, leading cause of cancer death in men (23%, bowel 15%, prostate 14%) and third most common in women. Maori women have the highest death rate from lung cancer of any female population in the world
- Males predominate. Females catching up

- 60% not resectable at the time of diagnosis
- 23% of all lung cancers are mixed
- Smoking:
 - > 90% are caused by smoking and are therefore preventable
 - 25% of lung cancer in non-smokers is due to passive smoking
- Types according to smoking status:

	% Smokers	% Non-smokers
Squamous Cell	98	2
Small Cell	99	1
Large Cell	93	7
Adenocarcinoma	82	18
Bronchioalveolar	70	30

- Presentation and Survival:

	Smokers	Non-smokers
Distant disease at presentation	> 50%	10%
Endocrine disorders	10 – 25%	5%
5 year survival	5%	17%

- Relative incidence changing rapidly:
 - ↓Squamous cell
 - ↑Adenocarcinoma (now more common than squamous cell in most countries)
 - ↑Bronchioalveolar carcinoma
 - Large cell constant

Presentation

- Fatigue 84%
- Cough 71%
- Dyspnoea 59%
- Anorexia 57%
- Pain 48%
- Haemoptysis 25%

Diagnosis

- Cytology necessary for management. Use the least invasive route (eg FNA of a neck node if there is one)
- Sputum cytology
- Bronchoscopy:
 - Can do washings, brushings, biopsy or lavage (to get more distal stuff)
 - If can't produce sputum sample, can nebulise with hypo-osmotic saline to induce sputum
 - 1% of transbronchial biopsy → haemorrhage or pneumonia
- Fine Needle Aspiration (FNA): good for peripheral tumours

Types of Lung Cancer

- Squamous Cell Carcinoma:
 - Most common form
 - Males > females, ↑ with age
 - Central tumour: presents late with invasion of lymph nodes
 - Can block airway → distal pneumonia
 - Pathogenesis: BPDE in smoke binds p53 mutational hot spots → mutation. Sequence of changes from squamous metaplasia to dysplasia to carcinoma in situ to invasive carcinoma
 - Macroscopic: Arises in major bronchus, grey-white hard granular neoplasm, central cavitation in large cancers, uninvolved lung shows smoking related pathology (eg emphysema)
 - Microscopic appearance: pink when stained (due to cytoplasm), keratin whirls and intracellular bridges (diagnostic), band in central cytoplasm, large irregular nucleus, nuclear pleomorphism, hyperchromatism (ie darker), coarse chromatin clumping, mitosis, large nucleoli, usually arranged in sheets
 - Complications: metastatic disease to lymph nodes, brain, liver and adrenals
 - Overall five year survival 10%

- Surgical treatment preferred: but may patients may have insufficient pulmonary reserve
- Small Cell Carcinoma:
 - = ‘Oat cell’ carcinoma
 - Central ⇒ poor prognosis
 - Very aggressive
 - Treatment: chemotherapy +/- radiotherapy – not surgery as will have metastasised
 - Neuroendocrine origin
 - Pathogenesis: BPDE in smoke binds p53 mutational hot spots → mutation
 - Macroscopic description: perihilar and surround large bronchi. Grey-white or haemorrhagic. May be more extensive microscopically
 - Microscopic appearance: small cells, scant cytoplasm (blue when stained – predominantly nuclei), ovoid, dense, hyperchromatic so nucleoli not usually seen, mitotically active, pleomorphic nuclei. Fragile → crushed causing blue streaks
 - Complications: metastatic disease to lymph nodes, brain, liver and adrenals
 - Two year survival 25%
 - Treatment: chemotherapy. Surgery useless unless palliative
- Large cell carcinoma:
 - Undifferentiated (the ‘waste basket’ category)
 - Central
 - White ⇒ desmoplastic
 - Microscopic appearance: Can’t tell cell of origin, contains giant cells, moderate amount of cytoplasm
 - Quite aggressive
- Adenocarcinoma:
 - Less common, Male = female
 - Occurs peripherally not centrally ⇒ more easily respectable (unless into pleura – poor prognosis)
 - Less association with smoking
 - Association with previous scarring (eg Tb)
 - Microscopic appearance: looks like it’s trying to form glands, ascini, desmoplastic stroma
- Bronchioalveolar carcinoma:
 - Distinctive variant of adenocarcinoma
 - Slowly crawls along bronchioles
 - Good 5 year survival but poor prognosis: drown in mucin
 - Type of adenocarcinoma
- Carcinoid tumour:
 - Low grade tumour derived from neuroendocrine cells
 - Occurs younger (mean is 45) than the more frequent bronchogenic carcinomas
 - Occur in lung, bowel, other sites
 - 90% Central types: 70% survive 5 years
 - 10% Peripheral types: rarely metastasise
 - Look like oat cell, but behave very differently. Grows by expansion rather than infiltration
- Mesothelioma:
 - Primary pleural tumours, including benign and malignant (also tumours of the peritoneum, tunica vaginalis and pericardium)
 - Benign mesothelioma does not produce pleural effusion and has no relationship to asbestos
 - Malignant mesotheliomas arise in either visceral or parietal pleura, *produce pleural effusion* (can be unilateral) and are related to asbestos. Drain effusion and re-xray (looking for lumpy pleura). Do cytology on fluid. Invades lung and often other thoracic structures. Presents in 5th to 7th decade, with lag after exposure of > 20 years. Diagnosis by imaging and biopsy. Poor prognosis. See Pneumoconioses, page 85.
- Adenosquamous carcinoma: rarer tumour with squamous and glandular features. Aggressive, bulky, peripheral tumour
- Pancoast tumour/syndrome: lung cancer (usually squamous) in the apex extending to supraclavicular nodes and involving 8th cervical and 1st and 2nd thoracic nerves → shoulder pain radiating in ulnar distribution. May also involve cervical sympathetic nerves and cause Horner’s Syndrome (ipsilateral enophthalmos – sunken eye, ptosis, miosis and dry skin)

Systemic Effects of Lung Carcinoma

- Often the presenting problem:

Type	Effect
Squamous cell carcinoma	Hyperparathyroidism (PTH) ($\rightarrow \uparrow \text{Ca}$ which may \rightarrow arrhythmias)
Small Cell Carcinoma	Cushing's Syndrome (ACTH) Carcinoid Syndrome Hyponatraemia (ADH)
All Types	Neuropathy and Psychosis (may be due to \uparrow neurotransmitter) Gynaecomastia (βHCG) in many poorly differentiated cancers

Prognosis

- No improvement in last 40 years
- 5 year survival for all cases 13%
- Prognostic factors:
 - Stage: most important factor
 - Age < 40 worse (diagnosed late)
 - Gender: female worse (diagnosed late)
 - Site
 - Size > 6 cm worse
- Staging:
 - Critical to prognosis and treatment decisions
 - Staging systems are regularly refined
 - TNM system (not usually used for Small Cell as these have usually metastasised by diagnosis):
 - T: Size and invasion
 - N: which mediastinal nodes are involved
 - M: no metastases or metastases present
 - TNMs are grouped to give stage groups ranging from IA to IV

Treatment

- Significant difference between Non-small cell and Small cell:
 - Non-small Cell:
 - Resection is the gold standard, but only 20% have resectable disease at diagnosis. Surgical studies are highly selected and not representative of the general population
 - Majority will require radiotherapy. Usually palliative, (eg for haemoptysis, pain or dyspnoea) can also be radical or adjuvant
 - Chemotherapy: not used much in NZ, standard treatment in the US. Cost a factor in newer agents. Myriad of dosing regimes, combinations, etc. Can be used prior to surgery/radiotherapy to control micro-metastases/improve operability, or palliatively. Cisplatin and Etoposide are the gold standards amongst the older agents
 - Small Cell:
 - 70 – 80% have metastasised at diagnosis
 - Very rapid doubling time
 - No place for surgery
 - Mainly managed with chemo +/- radiotherapy (makes a dismal outlook a bit better)

Sleep Apnoea

- See also:
 - Treatment of Insomnia, page 534 for Treatment of Insomnia
 - See also Tiredness, page 6

Sleepiness

- Varies according to circadian cycle: two sleep gates each day, 2 – 3 pm and 10 – 11 pm (correlates with \uparrow melatonin)
- Obstructive sleep apnoea is the most common cause of excessive sleepiness. \rightarrow MVA (driving drowsy is the same as driving drunk)
- Causes of \uparrow day time sleepiness:
 - Insufficient sleep (eg sleep restriction)
 - Obstructive sleep apnoea

- Central sleep apnoea: absent or diminished ventilatory drive. Variety of causes including neuromuscular and chest wall deformities
- Cheyne-Stokes Respiration: usually with advanced heart failure. Destabilisation of respiratory control centres
- Upper airway resistance syndrome (no actual apnoea)
- Periodic limb movements in sleep (PLMS: associated with restless leg syndrome) → fragmented sleep. Also hot legs at night, cramps. Occurs in renal failure and anaemia. Treatment: codeine or anti-Parkinson drugs
- Narcolepsy: Normal sleep at night and frequently going to sleep during the day. (Sleep study looks at daytime napping more than nighttime). Goes into REM sleep early. Equivalent to 48 hours sleep deprivation, vivid dreams (hypnagogic hallucinations), HLA linkage, affects young, twice as common as MS. Can also be complicated by cataplexy (sudden loss of muscle tone in response to emotional stimuli). Treatment: stimulants during the day
- Idiopathic hypersomnolence
- Drugs: alcohol, sedatives
- Psychiatric
- Hypothyroid
- Anaemia
- Normal breathing:
 - Inspiration: uses Genioglossus and other muscles to dilate trachea, and intercostals and diaphragm to create negative pleural pressure
 - Expiration: much more passive
- Normal changes during sleep:
 - Carotid bodies much less sensitive to ↑CO₂ and ↓O₂
 - ↓Intercostal & accessory muscle tone
 - → ↓tidal volume → ↓ventilation → ↑PCO₂ by 5 mmHg → ↑HR, flushed, warm periphery

Obstructive Sleep Apnoea Syndrome

- Pathogenesis: ↓muscle tone + anatomical factors (eg obese) + neural factors (eg stroke) → upper airway narrows → apnoea due to collapse → arousal → impairment overtime of sensitivity to daytime ↑PCO₂
- Epidemiology:
 - Prevalence = 4% of adult population
 - More common in:
 - Men and post-menopausal women
 - Middle age
 - In kids with facio-cranial syndromes
 - Short jaw
 - Alcohol users
 - Over weight
- Symptoms: Loud snoring, apnoea, daytime tiredness, early morning headache
- History questions:
 - When do you go to bed and when do you get up (sleep restriction)
 - Do you snore, in any posture (the norm with OSAS). Need witness accounts
 - Do you feel refreshed on waking
 - Where do you fall asleep (normal places but more often)
 - Other medical conditions: depression, anaemia, hypothyroidism, etc
 - Medications and when do you take them: can keep awake at night or make you sleepy during the day
- Consequences:
 - ↓concentration, ↓memory, ↑accident risk, ↓libido, premature mortality, hypertension, MI, CVA, precipitate respiratory failure in mild CORD
 - In kids: less apnoea (if there is apnoea then ?SIDS/epilepsy), more noisy breathing/restlessness, wake a lot at night, hyperactive during the day, growth delay (↓GH secretion due to ↓slow wave sleep)
- Diagnosis requires sleep study → Polysomnography. Measures muscle movements, airflows, O₂ and CO₂, EEG waves, eye movements, ECG etc during sleep

- Treatment:
 - Conservative:
 - Weight loss (did it start with weight gain?), smoke reduction, sleep posture modification
 - Nasal CPAP for moderate/severe: air splint prevents airway collapse through whole breath cycle. Need to titrate pressure
 - Treat allergic rhinitis
 - Medication: Sleeping pills make it worse – stop them
 - Dental devices
 - Surgery:
 - Kids – tonsils and adenoids.
 - Adults:
 - Mandibular advancement
 - Gastric bypass → ↓weight
 - Tracheostomy
 - Uvulopalatopharyngoplasty (UPPP) – but doesn't deal with all sites of occlusion and stops CPAP working

Miscellaneous Lung Diseases

- Goodpastures Syndrome (= Antibasement Membrane Antibody Disease – ABMA):
 - Simultaneous rapidly progressive glomerulonephritis and haemorrhagic pneumonitis
 - Present with renal failure and haemoptysis
 - Due to anti-basement membrane antibodies deposited along alveolar walls and in glomeruli (type II immune reaction)
 - Usually occurs in young men, treated with steroids and cytotoxic drugs
 - See also Goodpasture's Syndrome, page 214
- Alveolar Proteinosis: Peripheral alveoli filled with pink, granular, acellular material. No treatment, variable course, clears in a few years. Prone to infection so steroids worsen the condition by depressing the immune system. Bronchial lavage effective in acute episodes
- A number of vasculitis affect the lung. Eg Wegner's granulomatosis, allergic angiitis and granulomatosis. Also collagen diseases such as SLE and Rheumatoid arthritis
- Pulmonary Hamartoma: benign localised proliferation of normal tissue components (hyaline cartilage with respiratory epithelium, maybe fibrous tissue, fat, blood vessels). Usually found as incidental findings on X-ray
- Primary Pulmonary Hypertension: rare, usually in young women. Usually secondary to COPD, congenital or acquired heart disease, etc
- Langerhans cell: diagnostic cell seen in eosinophilic granuloma. = histiocytosis X and pulmonary eosinophilic granuloma. A large histiocyte with one bland folded nucleus, abundant eosinophilic cytoplasm with indistinct cell borders. Proliferative disorder of histiocytes. X-rays show multiple nodules scattered through both lungs
- Langhans giant cell: (not the same as Langerhans cell) multinucleated giant cell in granulomas, with nuclei arranged around the periphery of the cell in a horseshoe pattern
- Sequestration:
 - Extralobular: Congenital. Mass of lung tissue not connected to bronchial tree and outside the visceral pleura
 - Intralobar sequestration: usually acquired. Within the visceral pleura but not connected to the bronchial tree
- Differential of Solitary lung nodule:
 - Tumour: benign (bronchial adenoma or pulmonary hamartoma) or malignant
 - Tb
 - Sarcoidosis
 - Other granuloma: eg fungal
 - Haematoma (ie blood clot, eg in cavity following lung contusion)

Endocrine and Electrolytes

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History

- Symptoms widespread and often insidious
- Enquire about previous endocrine gland problems, surgery, etc
- Major symptoms:

- Changes in appetite and weight:

	↑Appetite	↓Appetite
↑Weight	Cushing's Syndrome, hypoglycaemia, hypothalamic disease	Hypothyroidism
↓Weight	Thyrotoxicosis, uncontrolled DM	Adrenal insufficiency (also GI causes and malignancy)

- Bowel:
 - Diarrhoea \Rightarrow hyperthyroidism or adrenal insufficiency
 - Constipation \Rightarrow hypothyroidism or hypercalcaemia
 - Sweating: hyperthyroidism, phaeochromocytoma, hypoglycaemia, acromegaly (also anxiety and menopause)
 - Subcutaneous thinning: either \downarrow androgens (old men and post-menopausal women) or \uparrow Cortisol
 - Amenorrhoea: \uparrow PRL (by only a little), \uparrow Cortisol (takes bigger increase), $\uparrow\uparrow$ hyperthyroidism
 - Nocturia: \downarrow ADH, or Diabetes from \downarrow insulin, \uparrow cortisol or \uparrow GH

Diabetes Mellitus

Diagnosis of diabetes

- 1999 criteria (ie textbooks out of date):
 - For Diabetes:

	Fasting Blood glucose	2 hours post glucose tolerance test
Diabetes (one or the other)	> 7.0 (was 7.8) mmol/l	> 11.1 mmol/l
Impaired Glucose Tolerance: IGT	< 7.0	7.8 – 11.1
Impaired Fasting Glycaemia: IFG (New category)	6.1 – 6.9	< 7.8

- For Gestational Diabetes:
 - Screening: at 28 weeks, non-fasting glucose load of 50g. If ≥ 7.8 should have gestational glucose tolerance test
 - Gestational Glucose tolerance test: 75 g load when fasting. Fasting level ≥ 5.5 OR 1 hour post glucose load of ≥ 11 OR 2 hour post glucose load of ≥ 8.5 (some say 9.0) \Rightarrow gestational diabetes.
 - 1 – 3 % of pregnancies have gestational diabetes
- Suggested regime for Screening for type 2 diabetes (Screening for type 2 diabetes, NZMJ 26 April 2002)
 - Test if > 5% of diabetes \Rightarrow Europeans over 50 and non-Europeans > 40 years of age
 - Yearly screening for anyone found to have IGT or IFG
 - Best to test with morning fasting glucose – although use random test with caution if conditions approach fasting or post-glucose load conditions
 - Finger prick testing not accurate enough
 - HbA1c not recommended for screening: different methods for testing and different normal ranges

IDDM – Type 1 (Juvenile Onset Diabetes)

- A chronic, progressive autoimmune process in genetically susceptible people, triggered by environmental factors
- Eventually cannot survive without insulin treatment. Ketoacidosis will develop unless insulin given (if any endogenous insulin then no ketones)
- Incidence up to 20 yrs: 10 – 15/100,000
- Prevalence: 0.25 – 3 % (10 – 15% of all diabetics)

- Peak age of incidence is 12 – but can present at any age (even after 40). Surges in presentation at 3- 4, starting school. ?Viral exposure
- 85 – 90% have no family history, but family history confers ↑ risk
- Antibodies:
 - Islet Cell Antibodies: risk of IDDM ↑ with ↑ level of ICA. Frequency in newly diagnosed IDDM is 65 – 85%. Frequency in population is < 0.5%
 - GAD (glutamic acid decarboxylase) antibodies: mildly specific antigenic enzyme released from islet cells when destroyed. Can test for these in prodromal stage
 - Insulin autoantibodies
- Acute presentation: hyperglycaemia (polyuria when glucose > 10 mmol/l, thirst, polydypsia), tiredness, weight loss. Also cramps, blurred vision, superficial infections. Ketoacidosis (now rare) also has nausea, vomiting, and drowsiness
- Kids presenting with mild hyperglycaemia: don't know if they will become IDDM or are MODY (Maturity Onset Diabetes Of The Young – ie Type 2). So when start insulin replacement back titrate (after stabilised) – type 1 may have honeymoon period until no endogenous insulin
- Currently being investigated for prevention in high risk individuals (ie have antibodies but not frank disease):
 - Cow's milk avoidance until 6 months of age
 - Early oral insulin therapy → autoimmune modulation
 - Nicotinamide (vitamin B) supplementation
- Treatment goals: stable blood sugar, prevent/monitor complications, promote normal growth and development, maintenance of normal weight

Investigations for both Type 1 and Type 2 Diabetes

- Glucose testing
- HbA1C. Any reduction worthwhile. Target is <= 7.0. Not all willing or able to achieve this
- Ketonuria
- 24 hour urine and measure C-peptide: a by-product of insulin production (have they any endogenous insulin – as long as replacement insulin hasn't → islet cell atrophy)
- Fundoscopy
- Lipids
- BP: want diastolic < 85 and systolic < 135 (especially for young or existing microalbuminuria)
- Microalbuminuria:
 - Nephropathy has two phases:
 - Normal blood pressure, creatinine, and urines but microalbuminuria.
 - Overt neuropathy: proteinuria, hypertension, ↑ creatinine and ↓ GFR
 - Normal level < 20 mg/24 hours. Microalbuminuria = 30 – 300 mg/24 hours. Dipsticks detect > 150 g/l (ie insensitive)
 - Microalbuminuria hard to test (needs 24 hr urine). So use albumin : creatinine ratio. Normal < 2.8 in men, < 4.5 in females in random test
 - If abnormal result then patients qualify for statins with cholesterol > 6 (normal threshold > 9)
 - See Diabetic Nephropathy, page 207

Complications

- Microvascular disease:
 - Due to thickened walls and laying down of advanced end glycosylation products
 - Eye disease: mainly retinopathy. After 30 years 80% have background retinopathy and 7 – 8% are blind (see Focal Ischaemic Retinal Disease, page 145). Also ↑ Sorbitol → cataracts.
 - Nephropathy
 - Neuropathy: peripheral and autonomic
- Macrovascular disease:
 - Coronary heart disease. Male diabetics have 2 times risk, females 4 times risk. Very high risk if other risks present (eg ↑BP, lipids, smoking etc)
 - Accelerated atherosclerosis (but lesions look the same)
- Kidney disease:
 - See also Diabetic Nephropathy, page 207
 - Onset of diabetes leads to:
 - Functional changes: ↑GFR, Reversible albuminuria
 - Structural changes: GBM thickening, mesangial expansion

- After 30 years, 30 – 40% have nephropathy. Unlikely if hasn't developed after 30 years (?some protective factors)
- Glomerular damage:
 - Nodular glomerulosclerosis. Acellular hyaline material (Kimmelstiel-Wilson Lesion): BM proliferates (ie collagen expansion of mesangial matrix) → sclerosed and fibrotic due to fibroblast infiltration → chronic renal failure. Earliest sign is microalbuminuria, due to pores getting bigger
 - Diffuse glomerulo-sclerosis: glomerular loop obstruction → necrosis (seen in hypertension or any end-stage renal disease)
 - Papillary necrosis: least blood supply → susceptible to ischaemia
 - Also pyelonephritis and reflux lead to kidney damage
- Immune deficiency: White cells affected when glucose > 14 mmol/l
- Neuropathy:
 - Glycosylation of nerve
 - Demyelination of nerve due to sorbitol accumulation in Schwann cells → slowed conduction
 - Peripheral sensory AND motor neuropathy (eg foot deformity, fallen arches)
 - Autonomic neuropathy leads to bladder problems, impotence, gastroenteropathy
- → Diabetic foot
- Special management in surgery, pregnancy and in intercurrent illness

Management of Diabetic Ketoacidosis or Hyperglycaemia

- Diabetic Ketoacidosis:
 - Signs: nausea, vomiting, thirst, abdominal pain, delirium, coma, acetone fetor, hypotension, tachycardia, metabolic acidosis (Kussmaul breathing), hyperosmolality
 - Treatment:
 - ABC, oxygen
 - IV crystalloid: may need 4 – 6 L. Will be severely dehydrated due to osmotic diuresis. Use normal saline, and reduce to hypotonic fluid once rehydrated and glucose < 15 mmol/l or if Na > 150 mmol/l
 - Potassium 20 mmol in first 6 hours then 10 mmol/hr according to plasma levels. If plasma K high then delay adding K until this has normalised
 - Insulin: actrapid 10 – 20 units. Resistance to insulin may suggest sepsis, insulin antibodies
 - Monitor acidosis. May need HCO₃
- Ongoing Management of Diabetes:
 - Acute symptoms are main reason for seeking treatment. But good control is more than just keeping out of trouble. Involves significant education
 - For Impaired Glucose tolerance and Impaired fasting glucose: lifestyle change and monitoring
 - Diet: ↓Saturated fats, low glycaemic index foods (sugar presented slower to liver, able to convert more to glycogen). Space out CHO more evenly throughout the day. If normal BMI and NIDDM try ↓ fats and ↑ CHO → may ↑ insulin release (BMI ~ level of insulin resistance)
 - Warn about effects on blood sugars of another illness (eg 'flu) → ↑blood sugars. Requires more regular monitoring. Don't just stop taking insulin if not eating.
 - Insulin:
 - Use fast acting for glucose peaks following meals, and long acting for basal rate (→ suppress gluconeogenesis overnight, etc)
 - Conventional regime: twice daily with both fast and long acting
 - Intensive regime: fast acting before each meal and long acting at night (= 4 jabs a day)
 - Diabetes Complications Control Trial (1993) examined 1441 volunteers (ie motivated) in two groups: conventional treatment (insulin once or twice daily) and intensive (3 or 4 times daily). Intensive therapy reduced risk in all categories, but ↑hypoglycaemia and some weight gain
 - Biguanides: eg metformin. ↑Insulin sensitivity, ↓gluconeogenesis, won't → hypoglycaemia. Nausea, vomiting, B12 malabsorption. Not in hepatic and renal disease or pregnancy. Not in hypoxic lung disease or cardiac disease
 - Sulphonylureas: ↑insulin release from β-islet cells (⇒ must have some left for it to work), ↓gluconeogenesis and glycogenolysis. Can → hypoglycaemia. Nausea, vomiting. Not in hepatic and renal disease or pregnancy.
 - Monitoring: HbA1C (normal < 6.5), daily blood sugars (before breakfast)

- Examples:

Case	Age	BMI	Fasting Gl	Post-prandial Gl	Ketones	Symptoms
1	50	35	6.5	12	-	-
2	50	35	12	14	-	Nocturia
3	50	25	12	14	-	-
4	50	18	12	14	+	Weight loss

- Case 1: Has more insulin than case 2 (insulin resistance is proportional to BMI, but her glucose is lower \Rightarrow more insulin) \Rightarrow earlier presentation than case 2. Treatment: diet + metformin (can \rightarrow diarrhoea secondary to malabsorption). If very overweight, check LFT
- Case 2: pancreas starting to fail
- Case 3: Weight loss may not do much. Are they CHO deficient (\uparrow CHO \rightarrow \uparrow insulin release)? May start with sulphonylureas. May need insulin sooner
- Case 4: Type 1/IDDM. Will be catabolic – need protein. Quick test with sulphonylureas but will need insulin at earlier stage

Thyroid

Assessment

- Clinical
- Biochemical
- The gland itself: enlarged, smooth, nodules, tender, etc
- Specific features: eg autoimmune (exophthalmos) or pituitary disease

Physiology

- TRH (hypothalamus) \rightarrow TSH (anterior pituitary) \rightarrow T3 and T4 (thyroxine \rightarrow peripherally converted to T3)
- T3 & T4 stored in thyroid follicles as thyroglobulin
- T3 exerts greater negative feedback on the pituitary. Only takes a 10% rise in fT4 to suppress TSH
- T3 is considerably more metabolically active (ie potent) than T4
- Liver converts T4 \rightarrow T3, as does kidney and muscle
- T4 goes down first in hypothyroid. Only measure T3 in hyperthyroid (as it drives symptoms)
- Bound in plasma to thyroid binding globulin
- Intercurrent illness: fT4 rises (liver stops converting T4 to T3 straight away – want to be catabolic) then T4 falls to subnormal levels as thyroid production slows. FT3 falls from onset. TSH slowly falls to subnormal levels with severe illness. (ie similar pattern to hypopituitarism)

Goitre

- Normal gland weighs about 30 g
- Nodular or diffuse?
- Can be hyper, eu, or hypo-thyroid
- Check size, shape, consistency, mobility
- Check for dysphagia, stridor, laryngeal nerve palsy (especially multinodular)

Thyroid Tests

- Free T4 and T3
- Plasma T4 (= bound T4 + free T4). False high in pregnancy, oestrogens (\uparrow TBG). False lows in NSAID, phenytoin, steroids, TBG deficiency
- Plasma TSH: Newer sensitive test means low levels can be measured \Rightarrow don't do TRH anymore
- If low T3 and T4 and normal TSH \Rightarrow ?pituitary failure
- Thyroid isotope scanning: to look for hot spots or cold spots
- Thyroid antibodies: raised in Hashimoto's and some Graves
- TRH test: Inject to test thyroid. If minimal increase in TSH then: Hyperthyroidism, multinodular goitre, thyroxine replacement, euthyroid Graves disease, autonomous thyroid nodule

Thyroid imaging

- Can use nuclear medicine, ultrasound (little routine use – can guide FNA), CT (not for intra-thyroid lesions but demonstrates extension and mass effects) or MRI. Only when suspicion of significant pathology

- Before scanning thyroid (with 99MTc pertechnetate), stop Iodine supplements (eg kelp), thyroxine, and angiography (contrast contains Iodine). Gland must be ‘hungry’
- Normal uptake is 1 - 3 %. If it takes up too much then hyperthyroid
- If diffuse uptake then Grave's. If multinodular then:
 - Cold nodules: 80% are cysts or regressive nodules. 20% are malignant. → FNA
 - Hot nodules: maybe with decompensation in rest of gland (\downarrow uptake due to \downarrow TSH)

Thyroid Eye Disease

- Retro-orbital inflammation and lymphocyte infiltration. May → optic nerve compression (→ colour desaturation and \downarrow acuity). Does not parallel degree of toxicosis
- At presentation, patient may be euthyroid, hypothyroid or hyperthyroid
- Management: Early referral. Check for keratitis with Rose Bengal eye-drops. Lubricant eye drops. Systemic steroids. Surgical and other treatments

Hyperthyroidism

- Symptoms: \downarrow weight, appetite \uparrow , frequent stools, tremor, irritability, hot intolerance, sweating, oligomenorrhoea, infertility
- Signs: Tachycardia, AF, warm peripheries, thyroid enlargement or nodules
- Additional signs in Grave's disease: exophthalmos (bulging eyes), lid lag (lid lags eye when following your finger descending slowly), vitiligo (growing patches of skin depigmentation due to \downarrow melanocytes), Pretibial Myxoedema (due to amyloid)
- Tests:
 - Progression:
 - TSH is suppressed first, while fT3 and fT4 normal \Rightarrow TSH is the most sensitive test. Suppresses with minor changes in fT4
 - fT3 rises next → mild symptoms
 - fT4 rises last → severe symptoms
 - Screening: fT4 and TSH
 - Severity: fT4 and fT3
 - Thyroid microsomal and thyroglobulin antibodies (only present in 80% of Graves at presentation)
 - If goitre, ultrasound, thyroid scan
 - Test visual fields, acuity and eye movements. Referral if positive. Steroids to reduce swelling
- Causes:
 - Grave's disease: F:M = 9:1.
 - Most common when < 50 (\uparrow multinodular goitre as you get older)
 - Probably results from Autoantibodies against TSH receptors. Check for hTSABs (human Thyroid stimulating antibodies)
 - May cause normochromic, normocytic anaemia, \uparrow ESR, \uparrow calcium, abnormal LFTs
 - Histology: large hyperchromatic nuclei, retracted thyroglobulin. Follicles same as in follicular carcinoma but carcinoma shows invasion of blood vessels
 - Toxic adenoma (= Plummer's Disease, Thyroid autonomy): a nodule producing T3 or T4 → hot spot on scan
 - Subacute Thyroiditis:
 - = De Quervain's Disease. Usually resolves in 3 – 6 months. If rapidly destructive then acute thyroiditis
 - = Inflammation of the thyroid secondary to:
 - Pregnancy: autoimmune. Gland may not be tender
 - Infection: coxaxvirus and mumps. Tender gland
 - Goitre (often painful). Usually self-limiting
 - If severe, then 3 phases:
 - Prodromal: may be 4 – 6 weeks long
 - Hyperthyroid: Release of preformed T3 and T4. TSH low. If very bad, fT4 will be 100 (normal = 10 – 24). \uparrow ESR in parallel with \uparrow T4
 - Hypothyroid/regenerating: For 2 weeks – 2 months. In proportion to severity of hyperthyroid phase. T3 and T4 will go very low (?gland exhausted), TSH will remain depressed for a while longer (ie resembles secondary failure)
 - Doesn't respond to carbimazole as it's releasing preformed hormone. Carbimazole stops formation of hormone. If mild then wait. If severe, then antagonise peripheral effects (eg propranolol). Steroids work but prolong illness

- Histology:
 - Neutrophils attack cuboidal epithelium (acute inflammation)
 - Thyroglobulin leaks out → granuloma formation
 - Resolution
- Post-partum thyroiditis: hyper or hypo thyroid. Hypothyroid may persist
- Other: Toxic Multinodular Goitre, self medication ($\uparrow T4$ but $\downarrow T3$), follicular carcinoma of thyroid
- Treatment:
 - Drugs: Thyourylenes: Carbimazole (40 mg/day PO for 4 weeks, then reducing every 1 – 2 months, withdraw after 18 months, 50% relapse) – or try block and replace strategy (ongoing carbimazole and replacement T4), propylthiouracil. Risk of agranulocytosis with Carbimazole and propylthiouracil
 - Toxic multi-nodular goitre and toxic adenoma unlikely to remit following drugs
 - Partial thyroidectomy: risk to recurrent laryngeal and parathyroids. May be hypo or hyper post surgery
 - Radioactive iodine (I^{131}): will ultimately become hypothyroid

Hypothyroidism

- = Myxoedema if severe
- Signs and symptoms:
 - Symptoms: Unhappy, no spark, \uparrow weight, constipation, cold intolerance, menorrhagia (excessive menstruation, $\downarrow T3 \rightarrow \downarrow$ oestrogen breakdown), lethargy, depression, dementia, \uparrow sleep. Symptoms insidious and subtle (T3 receptors in nuclei of nearly all cells – govern metabolism, modulation of other hormones, O₂ consumption, regulation of protein synthesis, etc, etc)
 - Signs: bradycardia, dry skin and hair, goitre
 - Signs of myxoedema (\uparrow hydration of subcutaneous tissue): non-pitting oedema (eyelids, hands, feet), yellowing of skin (myxoedema absorbs carotene. Sclera unaffected), thickened tissues, voice change (oedema in vocal chords), hirsutism, carpal tunnel syndrome
 - If severe: slow, slurred speech (swollen tongue, slow thought), intention tremour (cerebellar effects), muscle weakness and pain, deafness (reverses with treatment), paranoid ideation, agitation, coarser hair, hair stops growing but no diffuse hair loss, slowly relaxing reflexes (contraction normal, relaxation slow – not specific to hypothyroidism), plethora (deep red cheeks), hypotension, \uparrow ADH release → hyponatraemia, normocytic normochromic anaemia, but no neuropathy (except secondary to, say, carpal tunnel)
 - Myxoedema coma: presents in coma with history of above symptoms. Exclude: alcoholism, epilepsy, diabetes mellitus, use of sedative medication, or clear suggestion of a fall predisposing to a subdural haematoma. With myxoedema may find pleural effusion, ascites, myocardial oedema (\rightarrow arrhythmias), no focal neuropathies (unless concurrent CVA), possibly hypoglycaemia
- Progression of primary hypothyroidism:
 - Normal TSH is 0.35 – 5.3
 - Prodromal hypothyroidism:
 - TSH 4.0 – 10.
 - fT4 usually still normal. fT3 up marginally (failing gland \uparrow proportion of T3)
 - Partial hypothyroidism:
 - Early symptoms
 - TSH > 10 – 15
 - fT3 and fT4 falling, but may still be normal. fT3 falls later than fT4
 - Severe:
 - With time develop myxoedema
 - TSH > 60. fT4 < 6.0
- Diagnosis:
 - Screening and severity: fT4 and TSH
 - Primary: TSH rises with minor changes in fT4 (before clinical features).
 - Secondary (rare): Test fT4. TSH remains in normal range but is inappropriately low for the fT4 level
 - Thyroid antibodies: almost all have positive antibodies at diagnosis
 - Thyroid scan not indicated
 - Normochromic macrocytic anaemia
- Causes:
 - Spontaneous (autoimmune)

- Hashimoto's Thyroiditis: autoimmune disease, lymphocyte and plasma cell infiltration. Goitre. Usually older women. Often euthyroid + goitre. Invasion of polyclonal lymphocytes. Have oncocyes (cells with ↑ mitochondria)
 - Spontaneous primary atrophic hypothyroidism. Autoimmune, = Hashimoto's without the goitre, associated with IDDM, Addison's and Pernicious anaemia. F:M = 6: 1
 - Woody Thyroiditis (Riedel's Thyroiditis): fibrous replacement of the thyroid
 - Iatrogenic:
 - Following thyroidectomy and radio-iodine treatment
 - Drug induced: eg amiodarone (→ hypo or hyper), *lithium*, iodine in expectorants
 - Not deep x-ray treatment to face and neck (does lead to nodular goitre),
 - Juvenile:
 - Dyshormonogenesis: eg partial deficiency of peroxidase → gland hyperplasia → restore deficiency. Expect: mild ↑TSH, goitre and mildly hypothyroid
 - Agenesis/sublingual thyroid
 - Di George Syndrome. Absent thymus, hypoplasia of parathyroid glands, lymphopenia
 - TSH deficiency: isolated, panhypopituitarism, hypothalamic disease
 - 1% of Grave's go onto hypothyroidism
 - Iodine deficiency
 - High doses of iodine (eg ask about kelp)
- Treatment:
- Thyroxine. Takes 4 – 5 days to have any impact (ie not useful acutely). Review after 12 weeks. Adjust dose to keep TSH < 5 mU/L. $T_{1/2} = 7$ days so adjusting dose takes long time
 - Note: hypothyroid → slow drug metabolism
 - If pre-existing heart disease, introduce very slowly. Consider propranolol

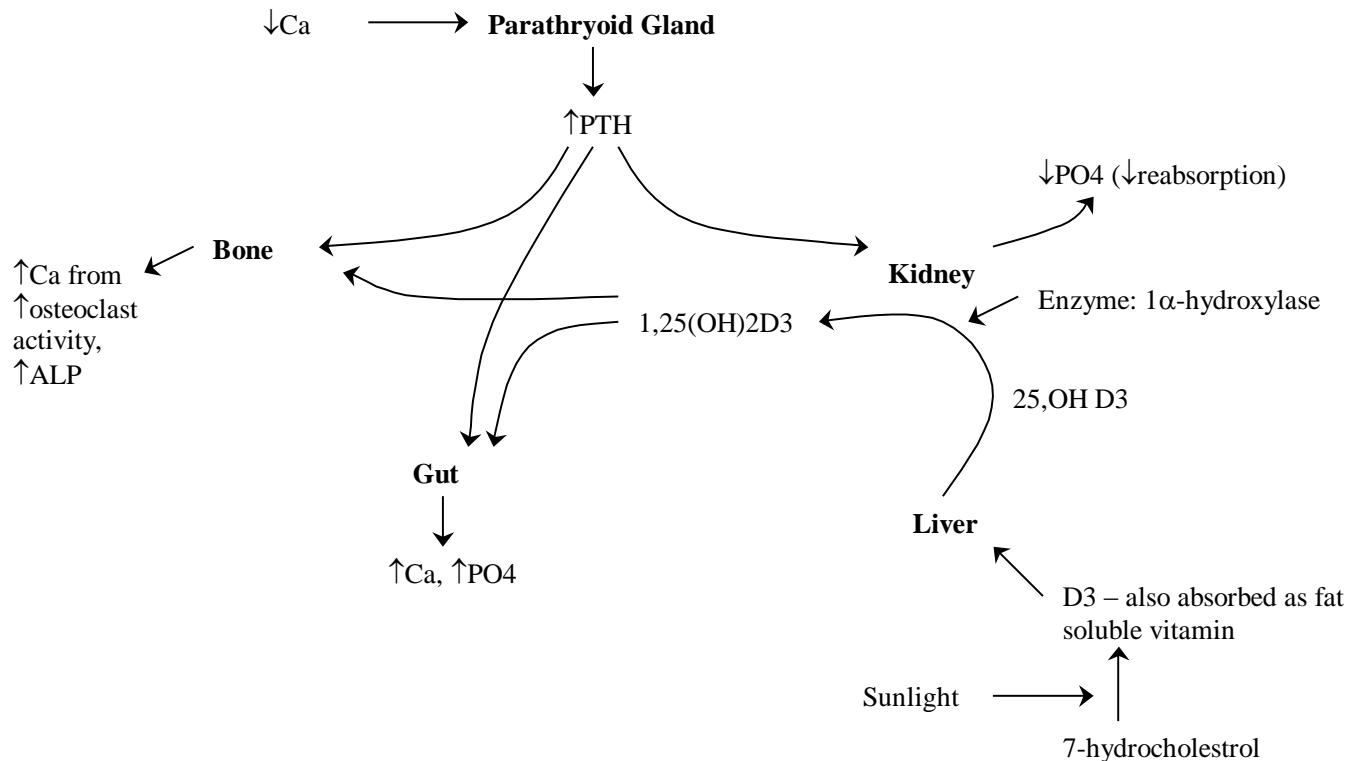
Thyroid Nodules

- Are common (occur in 10 – 60% depending on definition) but clinical malignancy is rare (2 – 10/100,000/year)
- Evaluation:
 - Presents with lump in lower neck
 - Age: young with nodules more likely to be cancer
 - Gender: Females have more nodules, male's nodule more likely to be cancer
 - Risk factors: radiation, family history, large solitary nodule bigger risk than many small ones
 - Symptoms:
 - Systemic: ↓weight and appetite, night sweats
 - Local: pain, stridor
 - Tests:
 - Usually normal thyroid function
 - Tumour markers: thyroglobulin, calcitonin
 - Imaging: Not specific: Cold spots – can be cancer but also normal. Hot spots unlikely to be cancer
 - US
 - FNA best
- Benign types:
 - Haemorrhage into a thyroid cyst: painful and instantly palpable
 - Adenoma: always follicular, encapsulated, universally benign. Usually cold on scan, may be hot
- Malignant:
 - **Papillary** Thyroid Cancer:
 - 60% of carcinomas
 - Have papillary (finger like) architecture with fibro vascular core
 - Metastasises to lymph nodes
 - May also have calcified bits ⇒ Psammoma Bodies (also found in meningiomas, serous cystadenoma of the ovary)
 - Prognosis: If extra-thyroid lesions then 62% survival @ 15 years
 - **Follicular** carcinoma: rarely multifocal, capsular invasion, metastasises via blood vessels. If gross invasion then 50% survival at 6 years. Hard to differentiate from adenoma on FNA
 - Anaplastic (undifferentiated carcinoma): highly malignant, old age, poor prognosis

- Medullary/C Cell carcinoma: parafollicular cells (\uparrow serum calcitonin). Usually part of Multiple Endocrine Neoplasia Syndrome (MEN)
- Treatment: near total thyroidectomy. If staging indicates high risk then radioiodine for remnant ablation
- Also lymphoma
- Multinodular Goitre:
 - With time, all thyroids have:
 - Anatomical heterogeneity: cold/fibrosed regions, hyperplasia, calcification, etc
 - Functional heterogeneity: various degrees of autonomy
 - If pronounced, then multinodular goitre:
 - Can be substantially enlarged with cystic appearance
 - Growth may \rightarrow haemorrhage \rightarrow tender
 - Treatment: Cut it out or thyroxine (slows it down)
- In addition to a tumour, a single nodule may be:
 - A hyperplastic nodule (ie physiological)
 - Multinodular goitre with a prominent nodule
 - Thyroglossal duct cysts (see Cervical Lumps, page 648)

Parathyroid

- Calcium metabolism:



- Hyperparathyroidism:
 - Primary: \uparrow PTH \rightarrow \uparrow Ca²⁺.
 - Usually detected as incidental finding. If symptoms: pain/fracture, renal stones, constipation, abdominal pain, depression. Also maybe dehydration, \uparrow BP, thirst, nocturia, stiff joints, myopathy
 - Associations: endocrine neoplasia (eg pancreas, pituitary, phaeochromocytoma and thyroid)
 - Causes: Single (90%) or multiple adenoma, carcinoma, hyperplasia
 - Tests: \uparrow Ca, \downarrow PO₄ (unless renal failure), \uparrow ALP, PTH raised or normal. CXR for 'pepper pot' skull and pelvis
 - Treatment: surgery

- PTH related protein (PTHrH): produced by some tumours – causes some of the hypercalcaemia seen in malignancy
- Secondary Hyperparathyroidism: $\downarrow \text{Ca} \rightarrow \uparrow \text{PTH}$. Causes: $\downarrow \text{Vitamin D}$ and chronic renal failure (see 210 – complications of chronic renal failure)
- Tertiary Hyperparathyroidism: continued secretion of PTH after prolonged secondary hyperPTH
- Hypoparathyroidism:
 - Primary HypoPTH. Eg after neck surgery. $\rightarrow \downarrow \text{Ca}$ and $\uparrow \text{PO}_4$, normal ALP. Associations with pernicious anaemia, Addison's, hypothyroidism, hypogonadism
 - PseudohypoPTH: Failure of target cell response to PTH. Round face, short metacarpals and metatarsals

Adrenal Cortex

- Produces:
 - Glucocorticoids: eg Cortisol - affects CHO, protein and lipid metabolism
 - Mineralocorticoids eg aldosterone
 - Androgens and oestrogens
- Cortisol:
 - Corticotrophin releasing factor (CRF from the hypothalamus) \rightarrow ACTH (from pituitary) \rightarrow Cortisol
 - Postulated that Cortisol inhibits a general or uncontrolled inflammatory response to tissue damage following insult. Raised in trauma, infection, severe psychiatric disease
 - ACTH production is inhibited potently by Betamethasone and Dexamethasone, Prednisone has intermediate potency and hydrocortisone (ie cortisol) has the lowest potency of these agents
 - Cortisol is excreted as urinary free cortisol
 - Morning level (2am – 8 am) is twice evening. Severe stress can override diurnal pattern
- Summary of best tests:

\uparrow Cortisol	\downarrow Cortisol
24 hour urine	\downarrow Renin
Low dose dexamethasone	Short Synacthen test

Cushing's Syndrome

- = Chronic glucocorticoid excess, either exogenous or endogenous (adrenal or pituitary neoplasm, or ectopic ACTH secretion)
- Signs: Tissue wasting, myopathy, thin skin, purple abdominal striae, easy bruising, osteoporosis, water retention, supraclavicular fat-pad (“buffalo hump”), predisposition to infection, bad wound healing, hirsutism, amenorrhoea, hyperglycaemia (30%)
- Tests:
 - Confirm source biochemically before looking radiologically. CT adrenal ‘incidentalomas’ are common \Rightarrow does not prove adrenal source of cortisol excess
 - Screening tests:
 - 24h urinary free cortisol (normal < 280 nmol/24 hr). If positive then high dose dexamethasone suppression test.
 - Alternative is low dose dexamethasone suppression test: give 1 mg po at midnight, check cortisol at 8 am (normal 450 – 700 nmol/L). False positives with depression, obesity and drugs affecting metabolism of dexamethasone (eg phenytoin, phenobarbitone)
 - Midnight cortisol *nearly* as good: but must do as an inpatient (need to wake to do it and be unstressed) – midnight is low point of diurnal cycle, if high then diurnal cycle depressed
 - Do high dose dexamethasone test (8mg) to determine type of Cushing's or if obese
- Causes and treatment:
 - Exogenous corticosteroid administration: reduce as much as possible. In asthma, use inhaled steroids
 - Cushing's Disease: (adrenal hyperplasia secondary to pituitary tumour, F > M, peak age 30 – 50). Some, but not normal, suppression of cortisol with high dose dexamethasone. Treatment: Surgical removal of pituitary adenoma
 - Adrenal gland adenoma or carcinoma: No suppression of cortisol with high dose. Undetectable ACTH. Treatment: surgical removal

- Ectopic ACTH production: especially small cell carcinoma of the lung and carcinoid. No suppression of cortisol with high dose dexamethasone. Plasma ACTH generally >250 ng/L. Hypokalaemic alkalosis is common. CT relevant areas (lung, pancreas, mediastinum, thyroid)
- Can block adrenal cortisol production with ketoconazole

Hypoadrenalinism

Addison's Disease

- Primary adrenal failure: Failure of gluco- *and* mineralo-corticoids – both have similar hypotensive and electrolyte effects (different mechanisms but additive)
- Pure glucocorticoid (eg cortisol) deficiency gives:
 - Hypotension (postural and resting BP) due to:
 - Depletion of plasma renin substrate (angiotensinogen): Cortisol is permissive to PRS production and lowers angiotensin levels and hence vascular tone
 - Reduced cardiac contractility and stroke volume due to sodium shift from ECF to ICF (with tendency to hyperkalaemia reciprocal to the Na cell influx)
 - These lead to secondary effects including ↓ renal plasma flow, reduced GFR and mild elevation in urea
 - Hyponatraemia results from:
 - Shift of Na⁺ from ECF into cells – K shifts out
 - Very high ADH (vasopressin) levels
 - Reduced renal free water clearance (in part from ADH excess and from the reduced GFR)
- Pure mineralocorticoid (ie aldosterone) deficiency gives:
 - Reduced Na uptake exchanging for K⁺ and H⁺ in renal distal tubule and in other epithelial surfaces (gut, sweat) → hyponatraemia
 - Secondary effects: hypotension, reduced GFR, clearly raised urea, raised K⁺
- With suspected Addison's, need to check for features of:
 - Mineralocorticoid deficit (few, but relate to salt depletion)
 - ACTH excess (hyperpigmentation)
 - A pituitary lesion (space occupying effects)
 - Hypopituitarism (gonadal, thyroid, prolactin or GH deficiency, PRL excess, ADH/vasopressin)
 - History of glucocorticoid medication
- Symptoms: very non-specific, weakness, abdominal pain, depression, 'viral illness', anorexia, D&V, nausea, pigmentation in palmar creases and buccal mucosa (takes ↑↑ACTH), arthralgia, myalgia, weight loss, nocturia, confusion, irritability, constipation, dehydration, dizziness (eg due to Na depletion → postural hypotension), hypoglycaemia (reduced gluconeogenesis). Lack of cortisol will obscure adrenergic effects of hypoglycaemia), diarrhoea, ↓libido, vitiligo (autoimmune mediated depigmentation of patches of skin). Not constipation or dehydration in pure cortisol deficiency
- Addisonian Crisis: tachycardia, fever, shock, coma
- Diagnostic tests:
 - Plasma renin (most sensitive indicator of mineralo-corticoid insufficiency)
 - Short ACTH stimulation test (Synacthen)
 - Better than 24 hr urine Cortisol (midnight cortisol test is equivalent to 24 hour urine).
 - Usually test at 0 and 30 minutes
 - Use long Synacthen test (0, 4, 6 hours) only when in doubt
 - If Cortisol doesn't rise then do prolonged ACTH stimulation test over 3 days (eg to differentiate between Addison's and prednisone suppression).
 - Basal (8 – 9 am) plasma ACTH will determine gland or origin (if high then primary, if low then secondary)
 - Basal (8 – 9 am) plasma Cortisol little help due to wide normal range
 - Test for adrenal antibodies and check for signs of Tb (eg calcification on Xray)
- Also test for: hyperkalaemia, hyponatraemia, hypoglycaemia, uraemia, mild acidosis, hypercalcaemia (?from pre-renal failure), normocytic anaemia, abnormal LFTs, ↑eosinophilia, ↓neutropenia
- Causes:
 - 80% idiopathic (autoimmune). Associated with Graves, Hashimoto's, IDDM, pernicious anaemia
 - Tb, metastases (insufficiency only after 90% of both adrenals destroyed)

Secondary Hypoadrenalinism: Pituitary Failure

- Tests for longstanding (ie > 6 – 8 years)
 - Short Synacthen test: measures adrenal atrophy
 - Insulin tolerance test: check for ACTH and cortisol release. Little data to judge normal range → not often used clinically

Adrenal atrophy from glucocorticoid therapy

- Occasionally short Synacthen test shows a delayed response
- Long Synacthen less convenient but more reliable

Steroid Medication

- Replacement doses for Cortisol:
 - Hydrocortisone = 15 mg per day, have to take 3 times a day due to short T½, and to avoid plasma peaks (→ side effects, eg osteoporosis)
 - Prednisone: 7 mg per day. Longer T½
 - Adjust by measuring cortisol (ie 24 hour urine cortisol). Replacement therapy does not usually suppress elevated ACTH
 - No abrupt changes in dose, increase in intercurrent illness. If vomiting then iv dose
 - Use Fludrocortisone for aldosterone replacement
- Withdrawal:
 - Withdrawal of long term prednisone needs to be done slowly (ie monthly reductions) due to atrophy
 - Signs of CG deficiency imply withdrawal is too fast

Hyperaldosteronism

- Excess of aldosterone independent of renin-angiotensin system
- Signs: hypertension, hypokalaemia, alkalosis, Na is normal or slightly raised
- Causes: >50% due to unilateral adrenocortical adenoma (Conn's Syndrome). Other causes include hyperplasia, carcinoma, genetic defect
- Tests: Test K 3 times on salt replete diet (no diuretics, etc for 4 weeks). If < 3.7 mmol, test for aldosterone or renin. Exclude renal artery stenosis (→↑BP and ↓K+), high renin (eg secondary to hepatic failure)
- Treatment: surgery and/or spironolactone

Phaeochromocytoma

- = Benign (usually) unilateral tumour in adrenal medulla producing catecholamines
- Signs: episodic hypertension, restlessness, anxiety, sweating, weight loss, tremor, cold feet, palpitations, extensive heart investigations
- Test: HMAA (breakdown products) in urine
- Treatment: surgery – careful management of BP before and after surgery

Pituitary Gland

- Anterior pituitary releases: ACTH, GH, FSH, LH, TSH, PRL
- Posterior pituitary releases: ADH, Oxytocin
- Under dominant tonic control (stalk failure → hormone failure): LH, FSH, GH, TSH, ACTH
- Under dominant inhibitory control (stalk failure → ↑): PRL
- Vasopressin (ADH): produced in hypothalamus, released in pituitary. Stalk failure → polyuria for a few weeks until ↑release in median eminence

Imaging the Pituitary

- Pituitary fossa is in the superior sphenoid bone, covered superiorly by the diaphragm sellae, with a central aperture for the infundibulum. The suprasellar cistern includes the infundibulum and the optic chiasm
- Pituitary is usually 6 mm in kids, 8 mm in men and postmenopausal women, 10 mm in women of child bearing age, 12 mm in pregnancy and postpartum. Gradual involution beyond 50 years old
- 'Pituitary bright spot': posterior pituitary is normally hyperdense. Lost in diabetes insipidus
- Normal pituitary fossa has a flat top, or concave (dips down)

- Microadenomas: < 10 mm, don't normally take up contrast. Are usually hormone secreting (that's why they're found)
- Macroadenomas: > 10 mm, most are not hormone secreting, found because of space occupying effect
- Sella and suprasellar lesions:
 - An empty sellae is due to herniation of the suprasellar cistern into the sellae → flattening of gland (with or without disturbance). Also secondary to hypophysectomy, post-radiation or infarction
 - Craniopharyngiomas: suprasellar tumours that may extend into the sellae. Kids and young adults. Cause pituitary insufficiency, visual impairment, hydrocephalus, hypothalamic disturbance
 - Meningiomas: MRI shows close meningeal attachment and enhancement post-contrast
 - Optic nerve gliomas: in kids. Extend along optic nerve

Hypopituitarism

- Causes: hypophysectomy, pituitary irradiation, adenoma (either functional or non-functional), other intracranial tumours, Sheehan's Syndrome (pituitary necrosis after post-partum haemorrhage), TB
- Check symptoms of:
 - Gonadal and GH (→ bone strength): early to fail
 - Thyroid: intermediate to fail
 - Adrenal: last to go.
 - Also look for PRL (need a little for LH peak to happen), vasopressin, space occupying lesions (test visual fields and for Oculomotor palsy)
 - ADH/Oxytocin only fail completely if hypothalamic tumour or major suprasellar extension
- Symptoms: insidious onset, afternoon tiredness, pallor, anorexia, ↓ libido (can be due to many illnesses to and ↑PRL), impotence, amenorrhoea, no menarche by 16, headache, depression, hypothyroidism, reduced body hair in males (due to hypogonadism – is also normal in older age – but not front baldness – that's due to androgens), intolerance of intercurrent illness and postural hypotension (hypocortisone), mild fluid retention (myxoedema and ↓cortisol → water retention), mild anaemia, pallor (yellow of myxoedema, and anaemia), also marked behavioural changes
- Signs: breast atrophy, small testes, ↓ muscle to fat ratio, ↓ hair, thin flaky wrinkled skin, postural hypotension, visual field defect
- Differentials: depression, dementia, subdural bleed (although more acute), slowly progressive tumour
- The age of presentation makes a difference:
 - Prepubertal failure slows growth, delays puberty
 - Post-pubertal failure reduces gonadal activity
 - Post-menopausal women: High FSH and LH would be normal. If FSH within normal range then → very sensitive test of early pituitary failure (if menopausal should normally be high)
 - Craniopharyngiomas are the commonest cause of pituitary failure in children, but can be found at any age
- Types of lesion:
 - Mostly hypopituitarism comes from non-functioning pituitary adenomas (adenomata)
 - But also craniopharyngioma, GH or prolactin secreting tumours
 - Most other causes are rare: pituitary apoplexy (a pituitary haemorrhage, mostly into a pre-existing tumour) and pituitary infarction (occasionally during delivery)
- Sites of tumour extension from the fossa
 - Suprasellar affects optic nerve
 - Parasellar affects III, IV and VI nerves
 - Infrasellar shows x-ray changes
- Tests:
 - CT/MRI, visual fields, basal T4, TSH and PRL, U&E (hyponatraemia), FBC (normochromic normocytic anaemia)
 - Triple stimulation test (unless heart disease or epilepsy): As inpatient with iv access, inject insulin, TRH and GnRH. Look for ↑GH, ↑Cortisol (due to ↑ACTH), ↑TSH, ↑PRL (due to ↑TRH)
 - LH and FSH insufficient on their own, without checking testosterone as well (may be ↓ due to ↑testosterone). Also LH & FSH tests are not sensitive enough to distinguish low from low-normal
 - Cortisol too variable to be a useful check of pituitary
 - Very high PRL indicates a prolactinoma, which can cause pan-hypopituitarism
 - An overnight Metyrapone test - give Metyrapone orally at midnight and measure plasma cortisol and its biosynthetic precursor at 8.30am. Metyrapone blocks the synthesis of cortisol leading to a build-up of 11-deoxycortisol and reduced negative cortisol feedback → a raised ACTH. Cortisol,

ACTH and 11-deoxycortisol all remain low in hypopituitarism or long-standing suppression of the HP adrenal axis by drugs

- Assessing severity:
 - Gonadal: Males – testosterone, LH and FSH. Females: menstrual history, LH and FSH
 - Thyroid: fT₄ and TSH
 - Adrenal: Short Synacthen test (false negatives possible) or urine free cortisol (not sensitive)
 - Growth Hormone: simple sample (after 10 am) or IGF1
 - Vasopressin: overnight urine concentration (osmolality)
- Treatment: Hydrocortisone and thyroxine. Maybe GH. Testosterone in men, Oestrogen for pre-menopausal women

Pituitary Tumours

- Symptoms caused by local pressure, hormone secretion or hypopituitarism
- Almost always benign adenomas
- Histological classification:
 - Chromophobe (70%): half produce PRL, some non-secretory, a few produce ACTH or GH
 - Acidophil (15%): Secrete GH or PRL
 - Basophil (15%): secrete ACTH
- Effects of pressure: headache (felt anywhere over head, local or general), bilateral hemianopia (initially of superior quadrants), III, IV or VI palsies, CSF rhinorrhoea (erosion through floor of sellae)
- Tests: as for hypopituitarism. Water deprivation test if diabetes insipidus is suspected
- Treatment: surgery (trans-sphenoidal or transfrontal). Hormone replacement. Bromocriptine for PRL secreting tumours. Radiotherapy (but side-effects common)

Prolactinaemia

- Physiology:
 - PRL has pulsatile and diurnal pattern: rises dramatically during sleep
 - Dopamine inhibits prolactin
 - PRL is raised by:
 - Oestrogen → slightly ↑PRL (ie women higher than men)
 - TRH → slightly ↑PRL (used in pituitary stimulation test)
 - T5 Dermatome stimulation → ↑PRL (but breastfeeding won't increase the size of a prolactinoma)
 - PRL rises through pregnancy
 - Drugs: most major tranquillisers (ie antipsychotics), Metoclopramide (Maxolon) therapy for nausea blocks dopamine → ↑PRL. Aldomet (alpha-methylDOPA) is the only hypotensive agent which increases prolactin (via dopamine depletion)
 - Can rise due to emotional or physical stress (including stressful venipuncture → artefact)
 - High in chronic renal failure
 - Hypothyroidism → ↑TRH → ↑PRL
 - Sarcoidosis
 - Post-pill amenorrhoea (if due to other causes usually resolves < 1 year)
 - PRL level is not effected by Progesterone or nausea
- Most common pituitary presentation. Presents early in women (amenorrhoea), late in men
- Symptoms:
 - Women: ↓libido, weight gain, apathy, vaginal dryness (due to hypooestrogen), amenorrhoea (very sensitive to ↑PRL, infertility due to ↑PRL → ↓LH peak, ↑PRL suppresses progesterone), galactorrhoea (will need to differentiate from breast inflammatory exudate – clear or green). If infertility, always check the man (cause of 1/3 of problems of infertility)
 - Men: impotence, ↓libido, reduced facial hair, local pressure effects, galactorrhoea (30%), mildly ↓testosterone (but asymptomatic). Not gynaecomastia (usually only in ↓testosterone or ↑oestrogen)
- Investigations: basal prolactin between 10.00 – 12.00 h (repeat 2 – 3 times), CT, MRI, assess pituitary function
- Management:
 - If tumour < 10 mm (unlikely to be seen on Xray): bromocriptine to restore fertility avoids complications of ↓oestrogen due to ↑PRL (could take pill instead). May → postural hypotension. Commence slowly otherwise nausea. Good prognosis. No known teratogenic effects of bromocriptine – but still withdrawn on becoming pregnant if possible

- Treat macroadenoma with surgery if bromocriptine fails to reduce size of PRL. But if pressure effects or pregnancy is contemplated then surgery. Monitor PRL
- Prolactin deficiency causes failure of lactation but has no other known ill effects. Deficiency is very rare

Acromegaly

- Usually presents between 30 – 50 years. Rare (3/million/year)
- Symptoms: insidious onset (look at old photos), coarse oily skin, large tongue, bossing of supraorbital ridge, ↑ shoe size and teeth spacing, spade-like hands, carpal tunnel syndrome, progressive heart failure, goitre
- Symptoms due to: **periosteal growth** (gigantism if the condition starts before closure of the bony epiphyses), **fibrous tissue growth** (→ skin thickening), **organomegaly** (eg cardiomegaly, hepatomegaly, splenomegaly, testicular enlargement), **cartilaginous growth** (↑ ears, nose, costochondral junctions), **neurological overgrowth** (→ peripheral neuropathy, exacerbated by the soft tissue swelling)
- Complications: DM, ↑BP, cardiomyopathy, ↑lipids, hypopituitarism
- Tests:
 - GH (highly variable – normally undetectable, spikes 10 times a day, mainly during deep sleep), ↑IGF-1 (insulin like growth factor) indicates GH secretion over the previous 24 hrs.
 - Oral glucose tolerance test. If GH doesn't fall then acromegaly, anorexia nervosa, poorly controlled DM, or Cushing's.
 - Tests as for pituitary tumour
- Treatment: trans-sphenoidal surgery if young. External irradiation for elderly. Somatostatin (Octreotide) if patient is not a good operative risk
- GH deficiency in children → growth retardation. One high GH level excludes deficiency. Take after sleep or exercise

Other Endocrine Problems

- Hirsutism: Male pattern of hair in a female. Common (10%). If normal menstruation then no increased testosterone production ⇒ benign. If abnormal menstruation then ?polycystic ovary syndrome with androgen hypersecretion or late onset congenital adrenal hyperplasia with deficiency of 21-hydroxylase enzyme
- Virilism: Male secondary sex characteristics in a woman. Rare. Amenorrhoea, deep voice, temporal hair recession, hirsutism. Refer for androgen secreting adrenal and ovarian tumours
- Galactorrhoea: may come with thyroid failure (primary or secondary), with a raised prolactin (prolactinoma, pituitary stalk section and especially drugs) and occasionally with acromegaly
- Gynaecomastia. Abnormal amount of breast tissue in males. May occur in normal puberty. Due to an ↑ in the oestrogen : androgen ratio. May result from liver disease (↓metabolism of oestrogen) or testicular tumours (↑oestrogens) or with hyperthyroidism. Commonest causes are drugs: eg spironolactone, cimetidine, digoxin
- Hypogonadism: Due to hypopituitarism, post-orchitis (eg from mumps), chemotherapy, irradiation, cirrhosis, alcohol (toxic to Leydig cells), various syndromes
- Impotence: Common in old age. Psychological causes are common (eg if clear stressor, or if morning erections still occur). Major causes: diabetes, drugs (diuretics, β-blockers, major tranquillisers, alcohol, antidepressants, cimetidine), hyperthyroidism, hypogonadism, ↑PRL, cirrhosis, cancer

Electrolytes

- See also ECG Abnormalities Due to Electrolyte Disturbances, page 27
- Arrest due to electrolyte abnormalities is uncommon except for hyperkalaemia.

Sodium Summary

- Low sodium:
 - Dilution: appropriate or inappropriate (SIADH)
 - Loss: sweat, GI, renal
- High sodium:
 - Retention: central or renal
 - Water loss

Hyponatraemia

Key Points

- Normal value of Na: 135 – 145 mmol/L
- Hyponatraemia is not a diagnosis – it is found in diverse conditions. Body Na may be low, normal or high. Relative water retention is a common factor
- Condition and treatment can be hazardous. If correct too fast then pontine demyelination
- Treatment must be slow and monitored closely. Treatment can range from water restriction or diuresis to sodium restriction or normal saline. Need to know underlying cause
- Don't use hypotonic fluids post-op unless Na is high. Eg dextrose saline – glucose absorbed very quickly post surgery → hypotonic

Symptoms

- The big boogie is underlying cerebral oedema. Bigger problem if abrupt onset. Rapid correction can cause central pontine melanosis
- Symptoms don't correlate well with [Na]
- Early: anorexia, headache, nausea, vomiting, muscle cramps, weakness
- Advanced: mutism, dysarthria, impaired response to verbal or painful stimuli, bizarre behaviour, hallucinations, asterixis, incontinence, respiratory insufficiency, spastic quadripareisis in 90%
- Far advanced: (too late to do much) decorticate or decerebrate posturing, bradycardia, hypo or hypertension, dilated pupils, seizures, respiratory arrest, coma, polyuria (central diabetes insipidous)
- Should always be a differential in post-operative coma

Aetiology

- Either Na depletion or water gain (usually water gain)
- Inappropriate water retention: eg drugs (most common – eg antiepileptics), ↑ADH, kidney or thyroid problems
- May be borderline hyponatraemic before (eg long term use of diuretics)
- Normal ADH will ↑ if ↑osmolality or ↓blood volume
- Operative stress or serious illness → syndrome of inappropriate ADH (in most people) → water retention (especially in women, smaller starting fluid volume). NB it's not really inappropriate – the body is making a justifiable physiological response: I'm stressed so conserve water rather than throwing it out.
- Ageing impairs fluid homeostasis → wider swings happen easily

Assessment

- History: fluid losses, *diuretics*, other medications
- Clinical findings: pulse, blood pressure, volume assessment, oedema, thirst, skin, input/output
- Laboratory:
 - Creatinine, urea, glucose, HCO₃, K, plasma osmolarity, urine Na and Osmolarity
 - Severe hyponatraemia is < 125 mmol/l: nausea, malaise, headache
 - < 115 mmol/l: convulsions
- Look for:
 - Low Na and ↓ serum osmolality
 - Urine osmolality higher than expected (>200 and usually > serum osmolality)
 - Urinary sodium higher than expected (> 30)
 - Normal pituitary, adrenal, cardiac, and renal function
- Clinically useful grouping (⇒ volume assessment critical):
 - Hyponatraemia with oedema: heart failure + diuretic, cirrhosis, nephrosis (impairment of water loss via increased ADH +/- Na loss)
 - Hyponatraemia with dehydration:
 - Urine [Na] > 20 mmol/l: Diuretics, Addison's Disease, Salt losing nephritis
 - Urine [Na] < 20 mmol/l: Vomiting, Diarrhoea, Skin loss
 - Usually rehydrate slowly with normal saline
 - Hyponatraemia with euvolaemia and reduced plasma osmolality:
 - Urine [Na] > 20 mmol/l: Chronic water overload (eg primary polydypsia, chronic SIADH – central or malignancy, etc)
 - Urine [Na] < 20 mmol/l: Acute water overload (eg acute SIADH, oxytocin for induced labour, etc)

- Treat with fluid restriction < 1000 ml/day, and treat underlying cause
- Complicating factors:
 - If plasma osmolarity is high then measure glucose. Hyperglycaemia → shift of water out of muscle cells: $\text{Na} \downarrow 1 \text{ mmol/L}$ for every 4 $\text{mmol/L} \uparrow$ in glucose
 - If osmolarity is normal then pseudo-hyponatraemia (eg hyperlipidaemia, hyperprotinaemia). An artefact: Na has been incorrectly measured in plasma volume rather than plasma water

Syndrome of Inappropriate ADH secretion

- = SIADH
- See Diabetes Insipidous, page 110
- Ectopic ADH Production (relatively rare): malignancies of lung, bronchus, brain, kidney, duodenum, pancreas
- Central production:
 - Cerebral infections, trauma, tumours, haemorrhage
 - Lung disease, eg pneumonia
 - Drugs, eg morphine, carbamazepine (anti-epileptic)
 - Can be seen in AIDS patients (?combination of above factors)

Common Scenarios

- Prolonged vomiting and rehydration with Gastrolyte – only contains 60 mmol/L Na
- If dehydrated (eg vomiting) and on diuretic, ADH still conserves water, but \downarrow Na retention so \downarrow [Na]. We preserve volume at the expense of osmolarity
- Serious post-operative problem. Especially women after elective surgery (eg gynaecology wards). Hypothesis: surgery → \uparrow ADH (eg due to pain), dextrose also given in belief that it slows catabolism and promotes healing – but together they lead to \downarrow [Na]
- Sample cases:

Case	1	2	3	4	5	6	7	8
Na	130	126	125	125	125	128	128	128
K	3.7	3.5	3.5	3.5	3.5	6.5	2.1	5.7
Creat	130		56	56	56	700	200	220
HCO ₃						15	40	3.0
Uos/Sos			0.4		1.6			
Sos						285		
Alb		16						
	Heart Failure + diuretic: too dried out	Nephrosis	Water overload	SIADH	Pseudo hyponatraemia or something osmotically active (eg \uparrow glucose)	Renal failure	Severe vomiting	Ketoacidosis

Treatment

- Principles:
 - Raise the sodium at a safe rate
 - Treat the cause
- Basic regimes:
 - If *volume depleted* (Renal/GI losses, diuretics, adrenal insufficiency): saline isotonic to the patient or normal saline. Extra Na will have a small effect but \uparrow volume → \downarrow ADH → excess water excreted
 - *Normovolaemic or oedematous* (SIADH, renal failure, polydypsia, oedema): Water restriction
 - If severe symptoms or if sodium < 110 then ?hypertonic saline. \uparrow Na by no more than 12 mmol per 24 hours: keep rate smooth. Key judgement is speed of infusion. No front loading. Animal studies show correction by > 14/mmol/24 hours → lesions in 71% of dogs. If no symptoms – maybe go slower
- Monitor 2 hourly. Manage in high dependency unit. Detect and treat hypoxia
- Adverse neurological consequences of rapid correction: myelin breakdown in the pons, patchy symmetrical lesions elsewhere in the brain. But risk of not treating acute cerebral oedema far exceeds the small risk of osmotic demyelination

- Maybe frusemide to ↑free water excretion

Dehydration or Volume Depletion

- Dehydration:
 - Often used loosely to describe a volume depleted patient
 - Correctly it refers to ↓intracellular water, following fluid shifts from ICF to ECF
 - Water is lost (either as pure water or as hypotonic fluid) → ↑osmolality and thirst
 - Treatment is water replacement (dextrose)
- Volume depletion:
 - Losses from the ECF (isotonic sodium) → ↓circulating volume
 - ↓BP, ↑tachycardia, ↓tissue turgor
 - Treatment is replacement of NaCl
- Dehydration and volume depletion can co-exist

Hypernatraemia

- Indicates ICF volume contraction
- Usually **not** due to ↑ total body sodium – total sodium is low, normal or high. Kidney is good at excreting excess Na (except if swamped – eg near drowning)
- Always means the patient is hyperosmolar
- Thirst and ↑ADH protect against hyperosmolality ⇒ don't see hypernatraemia where the thirst mechanism is normal and there is access to water
- Cellular dehydration → neurologic symptoms: lethargy, weakness, irritability, seizures, etc. Cerebral oedema if it is rapidly corrected
- Classification:
 - Water and sodium deficiency with water loss > sodium loss (ie lost hypotonic fluid), eg vomit, diarrhoea, sweat, osmotic diuresis (urine osmolarity not low), burns
 - With normal total body sodium (pure water depletion): unable to drink (old, babies, sick, etc), central or nephrogenic diabetes insipidous (see page 110)
 - With increased total body sodium: excess iv hypertonic saline, ingestion of sea water, mineralocorticoid excess (low sodium output) (⇒ expanded ECF)
- Treatment:
 - Chronic: may be asymptomatic even at 170 – 180 mmol/l due to adaptation by brain ⇒ gradual correction
 - If water deficit then:
 - Stop the water loss: give ADH, prevent osmotic diuresis, etc
 - SLOWLY give oral water or iv dextrose (Watch for hyperglycaemia, rate ~ 300 ml/hr. Add sodium if history suggests loss of sodium containing fluid and patient is not polyuric)
 - Aim for Na reduction of 1 mmol/L/hr and no more than 12 mmol/24 hours
 - If ↑Na: diuretics and give free water
 - Oral replacement is best if feasible

Diabetes Insipidous

- Symptoms: polyuria, dilute urine despite dehydration, polydypsia
- Central Diabetes Insipidous:
 - ↓Water resorption in kidney due to ↓ADH secretion from posterior pituitary → low urine osmolality (eg 150 mosmol/kg) despite dehydration. > 5/l per day urine requires hypothalamic damage as well as posterior lobe
 - Causes of central DI: head injury, tumour, metastasis, sarcoidosis, vascular lesion, inherited, drugs (eg phenytoin), idiopathic (50%)
- Nephrogenic DI:
 - Reduced response by kidney to ADH
 - Causes of nephrogenic DI: ↓K, ↑Ca, drugs (lithium), pyelonephritis, congenital, loss of medullary hypertonicity (eg renal interstitial disease)
- Tests:
 - U&E, Ca, plasma and urine osmolalities
 - Water deprivation test. Stop drinking then measure urine for 8 hours. If osmolality > 800 mosmol/kg then DI excluded. If diuresis continues, give nasal desmopressin and continue measuring

Potassium

- Normal value of K: 3.5 – 5 mmol/L
- Standard western diet contains ~ 70 mmol/day
- Shifts from ICF to ECF in response to:
 - Insulin deficiency
 - β -blockers
 - Acidosis
 - Cell necrosis
- Excreted in the distal tubule (K and H swapped for Na) under the influence of aldosterone. High HCO₃ excretion also \rightarrow ↑ K loss (eg alkalosis)
- Investigations:
 - H⁺
 - HCO₃: usually ↑ when K ↓ and visa-versa except when there is acidosis (eg renal tubular necrosis, diarrhoea)
 - Creatinine
 - Urinary K: > 20 mmol/L \Rightarrow renal K loss
 - Na: ↓ in hyperkalaemia, consider renal tubule disorder, ↓mineralocorticoid
 - Glucose
 - ECG (if widened QRS complexes give Ca). See ECG Abnormalities Due to Electrolyte Disturbances, page 27
- Key differentials: Diabetic ketoacidosis, renal failure

Summary

- Low:
 - Redistribution: alkalosis, β -agonists
 - Loss: GI, renal, thiazide or loop diuretics
 - ↓Intake (starvation, surgery)
- High:
 - Redistribution: acidosis
 - Massive cell lysis
 - ↓Excretion: DRUGS (eg ACE inhibitors), renal failure, hypoaldosteronism

Hyperkalaemia

- Causes:
 - Usually ↓ renal excretion
 - Shift from ICF (eg acidosis, massive cell lysis)
 - Low aldosterone: ACE inhibitors (instead use spironolactone), ↓renin (renal disease, NSAIDs, diabetes), poor adrenal function (eg Addison's)
 - Renal unresponsive to aldosterone: interstitial nephritis, K sparing diuretics
 - Renal failure: hyperkalaemia once GFR < 25 ml/min
- Signs: myocardial depression, peaked T wave, flat P wave, wide QRS, VF, diarrhoea, abdominal pain, muscle excitability
- Treatment:
 - If severe (> 6.5 mmol/L) consider:
 - Glucose 50 g + soluble insulin 10 U over 15 mins
 - IV calcium gluconate – stabilises myocytes but doesn't change K
 - β 2 agonist (salbutamol)
 - Dialysis if extreme
 - If moderate (5.5 – 6.5 mmol/L): Calcium resonium 15 g po (calcium binding resins), ↑renal loss through diuretics, mineralocorticoids

Hypokalaemia

- Causes:
 - GI losses (ECF volume contraction):
 - Vomiting, NG suction \rightarrow alkalosis \rightarrow ↑HCO₃ in urine and ↑aldosterone \rightarrow renal loss of K
 - Diarrhoea: \rightarrow K loss and metabolic acidosis
 - Urinary losses:
 - Diuretics: thiazides or loop

- Alkalosis (also shift to ICF if significant alkalosis)
- ECF normal or high: high aldosterone or hypermineralocorticoid (eg Cushing's)
- K shift into cells: metabolic alkalosis, insulin, β -adrenergics
- ↓Intake (starvation, surgery)
- Symptoms:
 - Muscle weakness, cramps
 - GI: constipation, ileus
 - Polyuria, nocturia
 - Urine – if ↑ volume then diuretics or osmotic diuresis, if not consider aldosterone action
- Signs: arrhythmias, PR prolonged, inverted T waves, U waves, VF, GI ileus, muscle weakness, hypotonicity, digoxin toxicity, alkalosis
- Treatment: May have large total body deficit (eg DKA). Replacement KCl up to 40 mmol/hour

Calcium

- See also Parathyroid, page 101

Summary

- If low Mg, then no ↑ in PTH in response to ↓Ca
- Low:
 - Hypothyroidism: abscess/gland destruction, ↓Mg, resistance to PTH (pseudo)
 - ↓Vit D: renal failure, malnutrition
- High:
 - ↑PTH: primary, secondary or tertiary
 - Paraneoplastic: PTHrH, bone metastasis
 - ↑Vitamin D: nutritional, ↑conversion (sarcoid)

Hypercalcaemia*

- Signs: "Bones, stones, groans and psychic moans". Also abdominal pain, vomiting, constipation, polyuria (Ca potentiates ADH effect), depression, anorexia, weakness, ↑BP, renal stones, cardiac arrest
- Most commonly:
 - Primary hyperPTH in the community
 - Malignancy in hospital
- NB: acidosis → H displaces Ca on albumin → ↑free Ca
- If albumin raised:
 - Urea raised → dehydration
 - Urea normal → cuffed specimen
- Albumin normal or low:
 - Phosphate low or normal (and urea normal): primary or tertiary hyperparathyroidism
 - Phosphate ↑ or normal:
 - ↑ALP: Bone metastases (most common primaries are breast, kidney, lung, thyroid, prostate, ovary, colon), sarcoidosis (↑Vitamin D conversion in the lungs), thyrotoxicosis
 - Normal ALP: myeloma, vitamin D excess, Ca supplements
- Treatment: if Ca > 3.5 mmol/l or severe symptoms:
 - Rehydrate and correct any hypokalaemia and hypomagnesaemia
 - Diuretics once rehydrated (frusemide, avoid thiazides)
 - Bisphosphonates (pamidronate): lower Ca over 2-3 days by inhibiting osteoclasts

Hypocalcaemia

- Normal value of Ca: 2.12 – 2.65 mmol/L
- 40% of calcium is bound to albumin. Adjust Ca for changes in albumin (0.025 per 1g of Albumin). Take sample uncuffed
- Symptoms: Tetany, depression, carpo-pedal spasm (wrist flexion and fingers drawn together), neuromuscular excitability (eg tapping over parotid causes facial muscles to twitch – Chvostek's sign)
- Causes of hypocalcaemia:
 - ↓Mg → ↓PTH → hypocalcaemia
 - Thyroid or parathyroid surgery
 - If ↑PO₄ then chronic renal failure (failure of Vitamin D conversion), hypoPTH or PseudohypoPTH
 - If PO₄ normal or ↓ then osteomalacia (↑ALP), over hydration or pancreatitis

Magnesium *

- Stored 65% in bone, 35% in cells
- Concentration generally follows Ca and K
- Excess:
 - Usually in renal failure \Rightarrow treat renal failure not magnesium
 - Symptoms: neuromuscular depression \rightarrow \downarrow BP \rightarrow CNS depression
- Deficiency:
 - Causes: severe diarrhoea, ketoacidosis, alcohol, TPN, with \downarrow Ca or \downarrow K (especially diuretics)
 - Symptoms: tetany (same as \downarrow Ca, \downarrow K gives weakness), fits, arrhythmia
- Treatment: Mg salts either po or iv

Chloride

- Anion Gap = Na + K – (Cl + HCO₃)
 - Usually 8 – 16 milliequivalent/l (measure of charge)
 - High Anion Gap: Ketoacidosis, lactic acidosis, renal failure, poisoning (salicylate, methanol, ethanol, ethylene glycol)
 - Low anion Gap: GI or GI loss of HCO₃, therapy for diabetic ketoacidosis, ingestion of HCl or NH₄Cl
 - Practical use limited – cause of metabolic acidosis obvious from history and observation
 - Most labs have deleted it from electrolyte profile
- Cl normally tracks Na except in metabolic acidosis. Eg severe vomiting: \downarrow HCl (\rightarrow hypochloraemic metabolic alkalosis) and volume depletion (\rightarrow kidney retains Na \rightarrow generation of HCO₃ and K depletion). Correction of alkalosis requires correction of volume, chloride and K

Acid-Base balance

Physiology

- Metabolism produces two acids:
 - Volatile: carbonic
 - Non-volatile: eg lactic
- Buffer systems:
 - H⁺ + HCO₃⁻ \leftrightarrow H₂CO₃ (H₂O + CO₂)
 - Henderson Hasselbach Equation:

$$\text{pH} = 6.1(\text{pKa}) + \log \frac{[\text{HCO}_3]}{0.03 * [\text{PCO}_2]}, \text{ or}$$

$$\text{pH} = 6.1(\text{pKa}) + \log \frac{\text{Kidney Production of HCO}_3}{\text{Respiratory Regulation of CO}_2}, \text{ or}$$

- Normal range for pH is 7.35 – 7.45 (=45 – 35 nmol/L of H⁺ ion)
- Range of pH compatible with life is about 6.8 – 7.8 = H⁺ concentration of 160 – 16 nmol/l
- Lots of other buffering systems
- Compensation:
 - Never complete
 - Respiratory: pH measured in the medulla. Compensates rapidly
 - Renal:
 - Alter bicarbonate reabsorption
 - Titratable acid excretion: organic buffers in tubules acidifies urine. Excretes 30 – 50% of acid produced each day
 - NH₄ excretion: formed in tubules, \uparrow takes days. Excretes 50 – 70% of acid

Respiratory Alkalosis

- Hyperventilation
- Causes:
 - Hypoxia
 - Lung disease: PE, asthma

- Anxiety
- Fever, sepsis
- Salicylate overdose: stimulates respiration, will subsequently develop metabolic acidosis
- $\downarrow \text{PaCO}_2$, $\uparrow \text{pH}$, initial alterations in $[\text{HCO}_3]$ are minimal, if it persists then kidneys compensate
- Compensation:
 - Acute: $\text{HCO}_3 \downarrow$ by 2 for each $10 \downarrow \text{PCO}_2$
 - Chronic: $\text{HCO}_3 \downarrow$ by a further 3 (ie total of 5) for each $10 \downarrow \text{PCO}_2$ [renal loss of HCO_3]

Respiratory Acidosis

- Hypoventilation
- Causes:
 - PCO_2 excretion lags production – eg severe asthma (initially asthmatics hyperventilate)
 - Pulmonary disease, muscular diseases, etc
 - CNS depression: primary or drugs/toxins
 - Asphyxia, smoke inhalation
- As $\text{PCO}_2 \uparrow$ then $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}^+ + \text{HCO}_3^-$
- $\uparrow \text{PaCO}_2 \rightarrow \downarrow \text{pH}$, initial alterations in $[\text{HCO}_3]$ are minimal, if it persists then kidneys compensate ($\uparrow \text{HCO}_3$ reabsorption, $\uparrow \text{NH}_3$ formation and excretion):
 - Acute: $\text{HCO}_3 \uparrow$ by 1 for each $10 \uparrow \text{PCO}_2$
 - Chronic: $\text{HCO}_3 \uparrow$ by a further 2.5 (ie 3.5 of total) for each $10 \uparrow \text{PCO}_2$
 - For example:

	PCO_2	HCO_3	pH
Uncompensated	80	24	7.10
Acute	80	28	7.17
Chronic	80	38	7.30

Metabolic acidosis

- Net gain of acid
- Causes:
 - Accumulation of acid (anion gap $> 18 \text{ mmol/L}$): $\uparrow \text{H}^+$ (ketoacidosis, lactic acidosis, ingestion of salicylates, methanol), renal failure (failure to excrete H^+)
 - $\downarrow \text{HCO}_3$ (anion gap $< 18 \text{ mmol}$): GI tract loss (eg diarrhoea), renal loss (eg \downarrow carbonic anhydrase), hypoaldosteronism
- Compensation:
 - Rapid: $\text{PCO}_2 \downarrow$ by 1.2 for each $\downarrow 1$ in HCO_3 (baseline = 24) - rapid
 - Slow: $\uparrow \text{HCO}_3$ reabsorption and $\uparrow \text{NH}_4$ excretion by the kidneys

Metabolic alkalosis

- Net loss of acid
- Causes:
 - Loss of H^+ :
 - Vomiting (suspect surreptitious if low Cl⁻)
 - NG suction
 - Renal loss (hyperaldosteronism)
 - Increase in HCO_3 reabsorption:
 - K depletion (Conn's, Cushing's, drugs, diuretics).
 - Volume depletion, eg \uparrow Aldosteronism $\rightarrow \uparrow \text{Na}/\text{H}$ exchange
 - Gain in alkali: eg NaHCO_3 administration
- Compensation:
 - $\text{PCO}_2 \uparrow$ by 0.6 for each $1 \downarrow$ in HCO_3 . Limited by hypoxia
 - Final compensation is by renal excretion of HCO_3 – requires correction of Cl⁻, K and volume

Summary of compensation rules

CO ₂	Change in HCO ₃ per 10 CO ₂	
	Acute	Chronic
Acidosis	↑	↑1 ↑ further 2.5 (total 3.5)
Alkalosis	↓	↓2 ↓ further 3 (total 5)
HCO ₃	Change in PCO ₂ for each HCO ₃	
	↑	↑0.6
Alkalosis	↓	↓1.2
Acidosis		

Mixed Acid/Base disorders

- Suspect if:
 - Clinical grounds
 - Compensation rules not obeyed
 - Normal pH but abnormal PCO₂ and HCO₃
- Examples:
 - Respiratory + Metabolic Acidosis: Pulmonary oedema + cardiac arrest
 - Respiratory + Metabolic Alkalosis: Over-ventilation + Nasogastric suction
 - Respiratory Alkalosis + Metabolic Acidosis: Septic shock or Salicylate OD
 - Respiratory Acidosis + Metabolic Alkalosis: CORD + Diuretic
 - Metabolic Acidosis + Metabolic Alkalosis: Renal failure + vomiting

Interpreting Blood Gas Results

- Arterial blood taken in 2 ml syringe containing heparin (to stop clotting) and transported on ice
- Look at pH: 7.36 to 7.44 is normal
- Look at PCO₂. If < 36 then hyperventilation. If > 44 then hypoventilation.
- Look at HCO₃. If < 22 then metabolic acidosis. If > 26 then metabolic alkalosis. But HCO₃ depends on PCO₂. So (to work out if its just compensation, or there is a metabolic problem as well as a respiratory one):
 - For acute changes (hours): a fall in PaCO₂ → a normal HCO₃ 2 less for every 10 mmHg ↓ in PaCO₂. A rise in PaCO₂ → normal HCO₃ 1 greater for every 10 mm Hg ↑ in PaCO₂
 - For chronic changes (days): a rise in PaCO₂ results in a normal HCO₃ 4 greater for every 10 change in PaCO₂

Base Excess

- Given on all arterial blood gas results
- = Concentration of titratable base when titrating blood or plasma with a strong acid or base to a plasma pH of 7.40 at PCO₂ of 40 mmHg at 37C
- Intent is to remove the impact of the respiratory component leaving just the metabolic component:
 - If +ive: metabolic alkalosis → deficit of non-carbonic acid
 - If -ive: metabolic acidosis → excess of non-carbonic acid
- BUT recognises normal compensation as an extra disturbance. May be useful for an anaesthetist (eg simple and acute disturbances)

Neuro-sensory

-
- References: Neurology, a 4th year Student Teaching Resource by Drs David Abernethy and Stuart Mossman, Wellington School of Medicine
 - See also Dementia and Delirium, page 439

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Neurology

- UMN = Upper Motor Neuron, LMN = Lower Motor Neuron

History

- Want to know the answer to two questions:
 - Where is the lesion (based on history and exam): Eg Weakness:
 - Upper motor neuron: motor cortex, internal capsule, brain stem or spinal chord
 - Lower motor neuron: nerve root, brachial/lumbosacral plexus, or peripheral nerve
 - Neuromuscular junction
 - Muscle
 - What is the lesion (based on history – mode of onset and progression)? Is it infarct, haemorrhage, inflammatory, tumour or degenerative
- Differentials:
 - Inability to walk: Parkinson's, spinal chord (demyelination, compression, disease due to ↓B12 or syphilis), cervical spondylosis, polymyositis, myasthenia gravis, Guillain Barre, hereditary motor and sensory neuropathy, MS, diabetic neuropathy, motor neuron disease, alcoholic neuropathy
 - Brief loss of consciousness: Stokes Adams attacks, VT, postural hypotension, hysterical unconsciousness, vasovagal syncope (fainting), epilepsy, CVA
 - Coma and Stupor: hypoglycaemia, Wernicke's encephalopathy, sedative or narcotic drug overdose, post anoxic coma, CVA, status epilepticus, meningitis, encephalitis, delirium, coning. See Coma and Stupor, page 130
 - Space occupying lesion: bleed, tumour, cyst, abscess, TB granuloma, AVMs, hydrocephalus

Physical Exam

- Hard to incorporate with rest of physical exam ⇒ do it on its own
- Tailor the exam to the clinical problem (full exam can take an hour)
- Avoid suggestion: rather than 'Is this sharp' or 'do you smell the perfume' say 'what do you feel/smell'
- Quick list:
 - Observe: including wasting and fasciculations
 - Cranial nerves
 - Tone
 - Power
 - Reflexes
 - Coordination
 - Sensation: position, vibration, pin prick, light touch

Mental State Exam

- Wanting to test:
 - Distributed cognitive function:
 - Attention/concentration
 - Memory
 - Word finding
 - Localised cognitive functions
 - Speech
 - Visuo-spatial
- If suspicious from history need assessment of the following:
 - State of consciousness: alert, drowsy, stuporose, comatose (assess with GCS)
 - Other observations from mental state exam (See Mental State Examination, page 414)
 - Orientation: date, their name, age, who are their relatives
 - Remote or long-term memory: phone number, Prime Minister, recent events in the news
 - Registration and Immediate recall: Memorise 3 objects, recall after 3 minutes. Repeat 4 or 5 digits in reverse
 - Others: abstract thinking, serial 7's
- Can use Mini-mental status test: but not sensitive to subtle impairments

Language

- If difficulty following instructions, appears confused, etc

- Requires assessment of spoken and written response to both spoken and written questions
- Observations: fluency, word finding, grammatical errors, understanding questions
- Naming objects: ask about whole object then parts – wrist watch and strap
- Repetition: No Ifs ands or buts
- Auditory comprehension: Increasingly complex commands, eg Close your eyes, touch your left ear with your right thumb and stick out your tongue
- Writing: write a simple sentence, their name and address
- Reading: read aloud

Cranial Nerve Exam

- 1: **Olfactory:** Smell. Not if doing general screen. Close eyes. Check each nostril patent then test (eg scented soap on ward). Poor smell common (smoking, allergies, ageing). Also in Alzheimer's, Parkinson's, MS, chemotherapy. Most serious association: frontal lobe tumour, presents with personality change, self-neglect, dementia
- 2: **Ophthalmic nerve:** lesions common and serious. Check if they normally wear glasses. Test:
 - Acuity: (use pinhole if they've forgotten their glasses). Test each eye separately
 - Visual fields: confrontational testing: first just hold hands in each visual field and ask what they see. Then wiggle one finger, then the other, then both, in all visual fields (or count fingers)
 - Red pinhead test: test for colour sensitivity – more sensitive than acuity (good for vague hemianopia). Loss of colour = "desaturation". Blind spot = "scotoma"
 - Hemianopia:
 - Pituitary lesion → bitemporal hemianopia (nasal retina affected). Bring red pin from affected field into normal – gain of red colour is convincing. Upper temporal field in one eye is typically affected first
 - Parietal lesion → visual inattention
- 3, 4, 6: Seeing double. Complicated to sort out
 - Look for ptosis
 - Smooth tracking: Fix on finger, draw H in the air, ask for report of diplopia, watch for one eye lagging or nystagmus (a few beats in extreme gaze is normal)
 - Examine pupils at rest, light reflexes and near reflex
 - Voluntary eye movement:
 - Look up, down, left, right. Often elderly have trouble looking up anyway
 - Cover test: look at target, cover one eye, does other eye move? Reverse. Shows which is fixing eye
 - If diplopia found, find field where it's maximal. Weak eye moves less; good eye overshoots. Use stick man drawn on tongue depressor
 - Problems locating target (overshoot and come back) → ?cerebellar
- 5: Trigeminal Nerve
 - Sensory 5th: Test light touch and pinprick in all 3 divisions on both sides (separate pathways in the brain stem). Test corneal reflex (early sign of lesion) – patient looks up, use cotton wool on cornea (more sensitive than sclera)
 - Motor 5th: jaw opening in midline (tests pterygoids). Jaw deviates to the side of weakness. Clench jaw and palpate masseters. Jaw jerk only if indicated
- 7: Facial Nerve. Wrinkle forehead and 'show your teeth' (not smile). Look for lower face weakness. Upper face (eg screw up eyes) better preserved in UMN, both similarly affected in LMN (eg Bell's palsy – can be due to HSV, onset in days, recovery in weeks/months, rarely parotid tumour). Note symmetry, fasciculation, and abnormal movements. Don't normally test taste
- 8: whispered voice at arms length, with patient's eyes close. Mask opposite ear by rubbing your finger and thumb together beside it.
- 9 (glossopharyngeal and vagus nerves): back of mouth, say ahh, uvula up in midline. Check swallowing. Gag normally not tested – if you do, test both sides. Unilateral absence abnormal, bilateral absence may be normal.
- 11 (accessory): shake and shrug shoulders. Observe sternomastoid and trapezius at rest for wasting, fasciculation, or dystonia. Look sideways, try to return head against resistance. Compare strength of shoulder shrug on each side. Rarely useful, unless confirming site or suspected lesion. Always test neck extension if diffuse muscle weakness – if abnormal indicates lesion above C1/C2
- 12: Hypoglossal nerve. Tongue. Examine at rest then protrude. If fasciculation → ?motor neuron disease. Deviates towards the weak side. Push tongue into check against your finger. Try rapidly alternating movements of protruded tongue or rapid la-la-la

INSERT Cranial Nerve Table

Motor Examination

- **Observation** for congenital maldevelopment, wasting, fasciculation and abnormal movements (tremor, chorea, myoclonus, dystonia)
- Assessment of **tone**: resistance to passive movement (must be relaxed). ↑Tone due to:
 - Rigidity (Basal ganglia): uniform resistance to slow passive movement, may be jerky (cogwheel rigidity). Affects flexors and extensors equally
 - Spasticity (upper motor neuron). Rapid passive movement → maximal tone to start with, decreases suddenly as muscle is lengthened. Most marked in flexors of arms and extensors in legs. Due to reflex contraction to muscle stretch
 - Clonus: maintaining stretch (eg of ankle plantar flexors) → further repetitive beating
- **Power**: compare between sides
 - Test in position where patient has mechanical advantage: you shouldn't be able to win then if its normal
 - Grade as follows:
 - 0: no contraction
 - 1: a flicker/trace of contraction
 - 2: active movement with gravity eliminated
 - 3: active movement against gravity but not against resistance
 - 4: active movement against gravity and resistance, but reduced power (covers wide range – can classify as mild, moderate or severe weakness)
 - 5: normal power
- Motor exam of the arms:
 - Observe arms at rest, then outstretched with eyes closed (check for drift – non-specific test). Look for wasting of 1st dorsal interosseous and abductor pollicis brevis
 - Assess tone at elbow (flexion/extension and supination) and wrist (flexion/extension) with slow and rapid movements
 - Arms (start at top and work down)
 - Shoulder abduction (deltoid, C5, axillary nerve). Arms out like chicken wings – push it down
 - Elbow flexion (biceps, brachialis, C5-6, musculocutaneous nerve) – pull me in
 - Elbow extension (triceps, C7, radial). Arm bent up in front - push me out
 - Wrist extension. (Extensor carpi ulnaris and radialis, C6-7, radial nerve). Extended 'cocked' wrist – push it down
 - Finger extension (extensor digitorum, C7). Fingers straight out – push them down just distal to MP joint
 - Finger flexion (flexor digitorum, C8). Try to uncurl curled up fingers
 - Abduction of index finger (ulnar nerve, T1, dorsal interosseous)
 - Abduction of thumb (median nerve, T1, abductor pollicis). Try and push raised thumb down into palm. Look for atrophy of thenar eminence
- Motor Exam of the legs:
 - Observation of legs: while standing, walking, lying down. ALWAYS observe posture and gait: movement of arms, stride length, broadness, smoothness. Stand with eye's closed and feet together (Romberg test). Look for wasting of tibialis anterior and small muscles of feet
 - Check for tone
 - Check for clonus. Flex hip and knee to 45 degrees, externally rotate hip, rapidly dorsiflex foot and hold. Two or three beats of clonus may be normal if symmetrical
 - Power in Legs (patient lying down):
 - Hip flexion (ilio-psoas, L1-2, lumbar plexus). Push down on raised straight leg
 - Hip extension (gluteus maximus, sciatic nerve, L5-S1). Lift ankle of straight leg
 - Knee Extension (quadriceps, femoral n, L3-4). Bend knee, try to push ankle in
 - Knee Flexion (hamstrings, sciatic nerve, L5 – S1)
 - Ankle dorsiflexion (tibialis ant peroneal n, L4 – 5): push on top of foot while toes raised
 - Ankle plantarflexion (gastrocnemius, sciatic nerve, S1 – 2): push on bottom of foot
 - Ankle inversion (tibialis ant & Post, peroneal and tibial n, L4 – 5). Patient bends foot in and try and pull it back
 - Ankle eversion (peronei, peroneal nerve, L5 – S1): Patient bends foot out and try and pull it back
 - Rapid leg tests:
 - If they can walk on their heals, then no foot drop (L5 or common peroneal)

- If they can walk on their tiptoes, then no S1 lesion (plantar-flexion)
- To test proximal leg function, crouch and stand up
- Differentiating Upper and Lower Motor Neuron lesions

	Upper	Lower
Tone	↑ (unless acute), Spasticity or Rigidity (mainly Parkinson's)	↓
Wasting	No	Yes
Reflexes	↑ (unless acute)	↓

Reflexes

- Key is for them to be relaxed
- Arm (Clench teeth if no response):
 - Biceps (C5/C6)
 - Triceps (C7)
 - Supinator (C5/C6)
 - Can also do finger reflex if suspect C8 lesion: tap your fingers while placed over outstretched fingers of face up hand. Often normally absent
- Leg (if no response, interlock fingers of both hands and pull just before tap)
 - Patella (hold knees up) (L3/L4)
 - Ankle (passively dorsiflex ankle) (S1). 3 ways: hand on dorsum of foot and tap hand, directly on Achilles tendon, or kneel on chair with foot hanging off, tap Achilles tendon (most sensitive)
- Grading reflexes:
 - 0: absent
 - +: just present
 - +: normal
 - ++: brisk normal
 - +++: very brisk
- Plantar responses: put patient at ease! Normal response is plantar flexion (down). If upper motor neuron lesion, big toe up and other toes fan out (Babinski). Not positive if withdrawal response (hip and knee flexion) due to over response
- Superficial Abdominal reflexes: Not tested routinely. Stroke lightly with sharp object in each quadrant towards midline. Normal reflex is contraction. Tires quickly

Co-ordination

- Rapid alternating movements of hand: supinate and pronate hand rapidly (dysdiadokinesia)
- Finger-nose-finger test. Not too fast (may mask intention tremour)
- Heel-knee-shin test
- Heel-toe walking: tests midline cerebellar vermis
- Romberg: tests dorsal column sensory loss (ie proprioception). Rare in clinical practice
- Important syndromes including ataxia:
 - Cerebellar haematoma: Sudden onset of progressive headache, vomiting, and inability to stand or walk. Later progressive drowsiness, lateral gaze palsy from pontine compression. Decompressive surgery can be lifesaving
 - Wernicke's Encephalopathy: Confusion, ataxia, nystagmus. 6th nerve palsy. On recovery: impaired short-term memory, confabulation. Common with prolonged vomiting, poor nutrition, not confined to alcohol

Sensory test

- Issue is where and why to test. What do you expect to find? Do this last so you have some idea what to look for. Very easy to suggest to patient
- Common scenarios:
 - Hemisensory loss: stroke, peripheral root and nerve lesion
 - Glove or stocking: spinal chord lesion or peripheral neuropathy
- Get patient to close eyes. Stimulate at irregular intervals so patient can't anticipate them. Test from abnormal to normal. Don't try to completely map – just test key boundaries
- Key Dermatomes:
 - Stand on S1
 - Sit on S3
 - Groin: L1

- Umbilicus: T10
- Nipple: T5
- T2 meets C4 on line connecting axilla: should be clear difference across this line in any lesion between T2 and C4
- Middle Finger: C7
- Position sense: hold big toe by the sides, explain which way is up and down, then test. Has low yield in practice. Try functional test: can they stand up with eyes closed?
- Vibration: 128 Hz fork. On bony prominences (what do you feel?). Move up until its positive. Bunion → medial malleolus → tibial tuberosity → anterior iliac spine. Test fingers for completeness. First sensation to go in progressive deterioration
- Pinprick: Use large safety pin and discard after use. Toes, fingers, face (no more unless suspicious, eg ↓ reflexes). Is it sharp or blunt? Can alternate sharp and blunt end to see if they can tell the difference. More reliable than light touch if both damaged
- Temperature: Not usually done if pin prick done
- Light touch (cotton wool)
- Others (not routine):
 - Two point discrimination
 - Stereognosis: recognising objects by their feel (coin, key, etc). Normal hand first
 - Graphesthesia: write numbers on the hand
 - Sensory inattention: touch sides separately and together – which is being touched?

Cognitive Functions

Localised Cognitive Functions

- Dominant hemisphere:
 - Speech, reading and writing
 - Calculation
 - Praxis (higher motor control of learned movement)
- Non-dominant hemisphere:
 - Neglect: visual, auditory, tactile
 - Dressing or constructional apraxia
 - Visuo-perceptual: object recognition (fragmented drawings) and faces (Prosopagnosia)
 - Prosody: Expressive aspects of speech

Attention/Concentration

- Depends on the reticular activating system, thalamus, frontal and medial temporal lobes
- Test: orientation in time and place, serial subtractions, spelling WORLD backwards etc

Memory

- Implicit: learned responses, reflexes and motor skills
- Explicit:
 - Episodic:
 - Left hippocampus: verbal, right visuo-spatial, faces, etc
 - Temporally specific personal experiences
 - Lost in diffuse brain disease (dementia) and bilateral limbic disease (amnesic syndrome)
 - Semantic:
 - Facts, concepts, words, meanings (eg object naming, what do you cut bread with, etc)
 - In the temporal neocortex (left)
 - Lost in dementia
- Working memory:
 - Very short term recall: words, numbers, melodies
 - Under frontal lobe executive control: important for dual task performance
 - Patients can have damage to just one of working or long term memory (eg Korsakoff)
 - Psychosis patients have normal working memory, but cannot make:
 - New memories (anteriograde): Word list learning
 - Retrieve long-term memories: recall public events, autobiographical details

Higher Cognitive Function/Executive Function

- Situated in the pre-frontal area (non-motor frontal lobes)

- Functioning best established from informants and observation
- Clinical features of frontal lobe lesions:
 - Poor planning: can't initiate and carry out a sequence of actions to complete a goal, can't do two things at once
 - Can't control impulses: irritable, irascible
 - Deterioration of personal relationships, social habits and hygiene
 - Dulling of curiosity and vitality, jocular, puerile
 - Lack energy

Common Peripheral Nerve Lesions

- Patterns of presentations:
 - Unilateral defined areas of weakness/sensory loss in hand or foot
 - Peripheral neuropathy
 - Paraparesis: weakness of both legs. Rare but critical. Usually spinal chord lesion
 - Muscle disease (rare): initial proximal pattern of weakness – neck flexion, shoulder abduction, hip flexion
 - Hemiparesis due to stroke: 1/day in Wellington (this one is not peripheral)
- Hand:
 - Common Lesions:
 - **Ulnar neuropathy:** Elbow compression → weakness of finger but not thumb abduction. Thumb adduction weak (paper test). Weakness of long flexors of 4th and 5th fingers. Wasting of interossei. Sensory loss on little finger
 - **Median nerve compression in Carpal Tunnel Syndrome:** weakness and wasting of abductor pollicis brevis, with numbness of palmar surface of fingers 1,2,3 and lateral 4. Tingling/pain which wakes at night
 - **C7 Radiculopathy:** pain from neck, shoulder, arm and forearm. Weakness of elbow, wrist and finger extension
 - **C6 Radiculopathy:** Weakens elbow flexion and wrist extension. Sensory loss of dorsolateral forearm, thumb and index finger
 - **Radial nerve (Saturday night Palsy):** Unable to dorsiflex the wrist or extend fingers or thumb.
 - Less Common Lesions:
 - Peripheral neuropathy: weakens small muscles of the hand, glove sensory loss
 - T1 root lesion: Weakness of small hand muscles, sensory loss on medial arm and often Horner's syndrome
- Leg:
 - **S1 Radiculopathy:** Pain in back, buttock, thigh, leg, and foot, numbness of the lateral border of the foot. Mild weakness of eversion and dorsiflexion, depressed ankle jerk
 - **L5 Radiculopathy:** Pain in back, buttock, thigh, leg, and foot, numbness of medial border of the foot and big toe, weakness of inversion and dorsiflexion. No reflex change
 - **Common peroneal nerve lesion from compression at the fibula head:** Painless, severe weakness of dorsiflexion and eversion, with normal inversion, and numbness on the lateral foot and dorsum of the foot. Maybe sudden onset with severe footdrop. Ankle jerk normal. 80% of nerve palsies causing foot drop recover over 3 – 4 months. Differentiating foot drop:

	Common Peroneal Lesion	L5 Lesion
Ankle jerk	OK	May be depressed (normally S1)
Inversion	OK	Weak
Eversion	Weak	

Brain Anatomy

- Revise it!
- Cerebro-spinal Fluid – CSF:
 - Made in coroid plexus on floor of lateral ventricles and roof of 3rd ventricle
 - Flow: Lateral ventricles → foramen of Munro (intraventricular foramen) → 3rd ventricle → Aqueduct of Sylvia → 4th Ventricle → via 3 foramen to cisternal spaces of subarachnoid space → arachnoid granulations → venous sinuses

Intracranial Haemorrhage

- Usually due to:
 - Trauma: typically extra/epi-dural or subdural

- Spontaneous (usually due to cerebrovascular disease): brain parenchyma and subarachnoid

Extradural Haemorrhage

- Due to head trauma, especially with skull fracture (although not necessary in children)
- Lentiform shaped arterial bleed (\Rightarrow high pressure \Rightarrow rapid progression)
- Skull fracture leads to one of:
 - Blood from middle meningeal artery forces its way between dura and inner table of skull (normally intimately related) – rapid, displacing cerebral tissue \rightarrow herniation
 - Laceration of dural venous sinus \rightarrow slow, delayed findings, less dense, less common
- Dura fixed at sutures so doesn't go past these (eg will be bounded by coronal and lambdoid sutures)
- Dura has two layers: the outer forming the internal periosteum of the calvarium, the inner forming the septae which compartmentalise the calvarium

Subdural Haemorrhage

- Following trauma: 50% also have a brain injury (swelling, contusion, laceration, etc)
- Bleed from bridging vein into the space between the arachnoid and dura mater (low pressure \Rightarrow slower progression)
- ↑Risk in old people due to relative cerebral atrophy
- Traverses right round the inside the calvarium: crescentic shaped bleed, very flat (may need to look carefully to distinguish from the skull)
- Most common location is over the lateral aspects of the cerebral hemispheres
- Poor prognosis due to large size and associated brain injury
- Classification:
 - Acute < 3 days
 - Subacute 4 – 21 days
 - Chronic > 21 days (eg minor injury in elderly, hypodense (blood broken down), lots of midline shift)
- If not detected, the haematoma undergoes organisation \rightarrow granulation tissue. This can rebleed

Subarachnoid Haemorrhage

- Into the space between the dura mater and pia mater – where CSF is
- Bleed may be focal, or diffusely spread through subarachnoid space (will flow into sulci and be bilaterally symmetrical)
- Incidence: 15 per 100,000
- Signs/symptoms: Sudden severe headache, loss of consciousness, meningism (neck stiffness, vomiting, photophobia, fever), maybe focal neurological signs, fundi
- Spontaneous: ruptured aneurysm (70%), Arteriovenous Malformation (AVM, 10%), hypertensive bleed, bleed into a tumour, hypocoagulable state
- Traumatic: injury to leptomeningeal vessels, rupture of intracerebral vessels, contusion, laceration
- Aneurysm:
 - Mostly situated on the circle of Willis (ie 40% are at the junction of the anterior cerebral artery and the anterior communicating artery)
 - Associated with connective tissue disorders (eg Marfan's)
 - Mostly saccular rather than fusiform
 - Saccular: due to ↓ elastic laminar (?congenital) = Berry Aneurysm. No muscle layer and thickened hyalinised intima
 - Fusiform: due to atheromatous degeneration
 - Mycotic: due to septic emboli – usually more peripheral in brain
 - Dissecting: may extend either from aortic dissection or from internal carotid artery (complication of angiography)
 - 85% are in the anterior circle of Willis. Posterior communicating artery \rightarrow unilateral 3rd nerve palsy (dilated pupil, ptosis, etc)
- Arterio-venous Malformations:
 - Localised developmental failure \rightarrow shunt from an artery to a vein \rightarrow gradually dilates \rightarrow distension of veins under arterial pressure
 - Most in the territory of the middle cerebral artery
 - Can present with haemorrhage or epilepsy
- Investigations: CT, CSF if CT not helpful and no risk of ↑ICP (make sure blood is not from a bloody tap)

- Treatment:
 - Analgesia, rest (maintain normotensive)
 - Rebleeding: 30% die from 1st bleed, 60% from rebleed (25% within 2 wks)
 - Clip or endovascular obliteration if GCS > 6
 - Vasospasm: 5 – 15% have stroke due to vasospasm (peak 3 – 10 days post bleed) despite all treatment. Cause: oedema around vessels → compression. Prevention with fluids, drugs and monitoring electrolytes
- Complications:
 - Acute: if intraventricular extension → ependymitis → obstruction of aqueduct → acute obstructive hydrocephalus. Also cerebral oedema and vasospasm of the affected artery (→ infarct)
 - Delayed: fibroblast proliferation in arachnoid space and at granulations → communicating hydrocephalus

Hypertensive Intracerebral Haemorrhage

- Mainly due to rupture of small penetrating vessels secondary to hypertension – which causes:
 - Hyaline arteriolosclerosis in small arteries and arterioles → weakening of vessel
 - Minute aneurysms
- Main sites are: Putamen, thalamus, pons, cerebellum
- → Haematoma → compression → brownish discolouration of surrounding tissue

How old is blood on a film

- On a CT:
 - < 24 hours: homogenous high density lesion, well defined margins, prognosis related to size of clot
 - Then oedema develops, increasing the mass effect, less homogenous
 - For the first week is hyperdense cf brain tissue (clotting → contracting)
 - 2 – 3 weeks isodense
 - 3 – 4 weeks is hypodense cf brain tissue. Breakdown of haemoglobin → ↑ osmotically active particles → water diffuses in.
- On MRI:
 - T1: fluid is black: hypointense
 - T2: fluid is white: hyperintense
 - If contrast enhancement → ring enhancement, then either an abscess *or* metastatic deposit

Stroke

- = The acute onset of focal or global neurologic deficit presumably of vascular origin lasting > 24 hours (WHO). This includes ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage
- Aetiology:
 - Risk in NZ in 65 – 74 is 1:100, in 85+ is 1:30
 - 80% due to atheroma, thrombosis and embolism, especially following heart (recent MI, AF, RF disease) or vessel pathology
 - Nearly half the people having a new stroke are already in institutional care or needing help with daily activities
 - 25% of strokes are in people who have had a previous stroke
- Differential to stroke: TIA, Migraine, Trauma, space occupying lesion (sub-dural haematoma, tumour, abscess), infections, hypoglycaemia, delirium, MS and spinal chord pathology/injury
- Isolated signs seldom due to a TIA or stroke: dizziness, unconsciousness

Site of Lesion

- Site of lesion:
 - 75% hemisphere
 - 25% posterior circulation
 - 20% lacunar
- Pathophysiology: Brain has high and constant need for blood supply
- Signs of cerebral involvement:
 - Dominant hemisphere: language disorder (dysphasia, middle cerebral artery)
 - Non-dominant hemisphere: disorders of knowing (agnosia) and doing (apraxia), visual or sensory neglect
 - Loss of integrated cerebral function (eg cognitive impairment, memory, abstract thought)
 - Failure of inhibition of lower centres (eg spasticity and urinary incontinence)

- Seizure activity: abnormal electrical activity in brain tissue around areas of ischaemia
- Hemianopia
- Four classes:
 - Total anterior circulation infarction (TACI. Anterior = Carotid artery \Rightarrow anterior and middle cerebral arteries): language or visuospatial disorder (depending on side) + homonymous hemianopia + motor deficit in two or more of face, arm or leg
 - Partial anterior circulation infarction (PACI): 2 of 3 of TACI criteria
 - Posterior circulation infarction (POCI. Posterior = Basilar artery \Rightarrow posterior cerebral artery): variety of presentations, including ipsilateral cranial nerve palsy with contralateral motor and/or sensory deficit, isolated cerebellar dysfunction, isolated homonymous visual field defect
- Common lacunar syndromes (small deep white matter infarcts):
 - Pure motor hemiparesis
 - Pure sensory abnormality
 - Ataxic hemiparesis
 - Sensori-motor stroke
 - Dysarthria and clumsy hand
- Signs of brain stem involvement:
 - Diplopia, bilateral weakness or numbness, vertigo, ataxia
 - Brain stem syndromes: *

Syndrome	Structures Affected	Symptoms
Medial Medullary due to Ant. Spinal or Vertebral artery	Hypoglossal nerve (12) Medial lemniscus Pyramid	Atrophy and paresis of tongue, deviates to ipsilateral side Contralateral loss of discriminative touch and proprioception Contralateral hemiparesis
Lateral Medullary, due to Vertebral, PICA, maybe AICA	Spinal trigeminal n. & tract Spinothalamic tract N. ambiguus Inferior cerebellar peduncle Vestibular n. Dorsal motor n. Descending sympathetic fibres	Ipsilateral loss of pain/temperature on face Contralateral loss of pain/temperature on body Loss of gag reflex, dysphagia, dysarthria, swallowing problems Ipsilateral ataxia Nystagmus, vertigo Vomiting Ipsilateral Horner's syndrome
Basal Pontine Syndrome, due to Basilar and pontine arteries	Abducens Facial Medial lemniscus Corticospinal tract	Ipsilateral medial deviation of the eye Ipsilateral paralysis of face Contralateral loss of discriminative touch and position sense Contralateral hemiparesis
Mediobasal mesencephalic syndrome due to aneurysm of posterior Circle of Willis or Basilar	Oculmotor Edinger-Westphal Corticospinal tract Red nucleus	Ipsilateral outward deviation of eye Ipsilateral dilated pupil, no light reflex Contralateral hemiparesis Contralateral cerebellar ataxia

- Transient Ischaemic Attacks (TIAs):
 - 30% of untreated TIAs eventually have a stroke, aspirin reduces this by a quarter
 - Presence of carotid bruit not very sensitive for stenosis (ie can have stenosis without it, may not have significant stenosis with it)
 - Surgery for carotid stenosis giving TIAs: beneficial if stenosis $> 70\%$, $\rightarrow \downarrow$ risk of ipsilateral stroke. Other studies less variable (NNT if asymptomatic = 17, if symptomatic then 6 – 7)
 - Angiogram morbidity = 1.5%, surgical morbidity 1.5 – 6.3% (if not vascular trained)

- Also consider multi-infarct dementia

Management

- Investigations:
 - FBC: exclude polycythaemia and anaemia. Do electrolytes and renal function
 - ESR: exclude vasculitis
 - Glucose
 - ECG/CXR for heart disease, AF
 - ?CT – 5% don't have a stroke, also exclude haemorrhage before antithrombotic treatment, and to assess for carotid surgery (>70% stenosis)
- Treatment:
 - Aspirin → small improvement in outcome if not haemorrhagic
 - Heparin has a negative effect: although beneficial for DVT prophylaxis
 - Warfarin anticoagulation if mitral stenosis or AF
 - tPA if within 4 hours and there is visible evidence of infarct covering < 1/3 of MCA territory on CT
 - Immediate anti-hypertensive therapy only if hypertensive encephalopathy is suspected (will have papilloedema)
 - Assessment of swallowing by a speech-language therapist: 40% of hospitalised stroke patients have swallowing problems, can → aspiration. Gag reflex is not sufficient to indicate normal swallowing. Nil by mouth until assessed (ie for 12 – 24 hours) unless clearly dehydrated
 - Watch for cerebral oedema over next 24 hours if large stroke. Restrict fluids, iv mannitol
 - Early rehabilitation: turning to prevent bed sores, limiting bed rest
 - Assessment for depression (common following stroke) and urinary incontinence

Prognosis

- After 6 months, 1/3 are dead, 1/3 have moderate disability, 1/3 have good recovery
- Poor prognosis if haven't started to make a good recovery after 2 weeks (acute assessment not reliable)
- Risk factors for poor prognosis: prior stroke, persistent incontinence, cognitive/perceptual deficits, poor previous functional status or social supports, poor sitting balance

Vascular Pathology

- Primary intra-cerebral haemorrhage:
 - Eg Sub-arachnoid haemorrhage or Intra-cerebral haemorrhage related to trauma
 - Due to high blood pressure or lobar haemorrhage (?due to amyloid deposition in vascular walls)
- Ischaemic stroke:
 - Thrombotic: occlusion – depending on collateral flow
 - Embolic stroke
 - Other: vasculitis, cerebral venous thrombosis, carotid artery dissection, etc
- Extent of infarction depends on:
 - Adequacy of collateral flow (via circle of Willis). Little/no collateral flow for the deep penetrating vessels supplying the thalamus, basal ganglia, and deep white matter
 - Presence of previous occlusive lesions
 - Location and rapidity of the occlusive process
- Infarcts are of two types:
 - Haemorrhagic (red) infarcts
 - Non-haemorrhagic infarcts: pale, bland, anaemic

Thrombotic infarction

- Arterial occlusion usually due to in-situ thrombosis over a plaque, or emboli
- Most common sites for atherosclerotic involvement are:
 - Carotid bifurcation
 - Origin of the middle cerebral artery
 - Either end of the basilar artery

	Pathology	Imaging
< 24 hours	Cytotoxic intracellular oedema	CT: normal. Subtle loss of grey-white matter interface. Little/no mass effect MRI more sensitive than CT in first 24 hours. See cortical thickening and loss of sulci MRI, T2: ↑ signal intensity MRI, T1: ↓ signal intensity
1 – 7 days	Tissue necrosis, maximal intracellular oedema, blurring of grey-white interface, tiny haemorrhagic infarcts	CT: hypodense, homogenous area with sharp margins. Variable mass defect MRI, T2: hyperintense
7 – 21 days (Subacute)	Resolving oedema. Marginal capillary ingrowth. Progressive liquifications	CT: Isodense surpigenous bands and nodular regions develop in the hypodense infarct. Infarcted white matter does not show density change. Contrast → ring enhancement MRI: loss of previous hyperintensity.
Chronic	Phagocytic removal of necrotic tissue. Cystic cavitation (esp in white matter). Gliosis (proliferation of fibrillary astrocytes → glial membrane)	CT and MRI. Lesion becomes homogenous. Approach density of CSF. Gliosis → contraction. Dilation of adjacent ventricle. Overlying cortex is atrophic, enlarged sulci and cisterns. Stable by end of 3 rd month.

- Healing in the brain: don't want scarring as the remaining tissue doesn't need protection (it's still within the skull) and scar contraction would damage surrounding tracts. So instead of scarring, you get gliosis and cavity formation

Embolic Infarction

- Mural thrombosis → emboli. Most common sources are plaques within the carotid arteries and cardiac mural thrombi
- Most commonly affects middle cerebral artery
- Embolus responsible for ischaemia lyses within 1 – 5 days → reperfusion into ischaemic brain (lost the ability to autoregulate)
- This leads to ↑ perfusion, especially of grey matter and basal ganglia (lots of capillaries). ↑Oedema (would be ↓ if thrombotic) → ↑mass effect. Cortical petechial haemorrhages. If these are extensive and merge → haemorrhagic infarct
- CT: previously hypodense become iso/hyper dense

Haemorrhagic Infarcts

- Usually secondary to embolic infarct
- Result from high reperfusion pressure, or following anticoagulation in thrombotic infarcts (eg heparin)
- May develop within 21 days following an embolic infarct
- Difference between haemorrhagic infarct and Intracerebral haemorrhage:

Haemorrhagic infarct	Intracerebral Haemorrhage
Inhomogeneous	Homogeneous
Wedge-shaped or rectangular	Round/Oval
Indistinct border	Sharp margins
Predominantly cortical	Predominantly white matter

Haemodynamic Infarcts

- ~ Border zone infarcts
- Vaso-occlusive disease + disturbed autoregulation → temporary uncompensated decrease in perfusion pressure
- Affects watersheds between vascular territories (may →haemorrhagic infarct), especially between the middle and anterior cerebral arteries
- Can lead to transient ischaemic attacks and infarction

Lacunar Infarcts

- Hypertension → arteriolar sclerosis of the deep penetrating arteries of the:
 - Middle cerebral artery → basal ganglia and internal capsule

- Posterior cerebral and basilar communicating arteries → mid-brain and thalamus
- Arteriolar sclerosis → hyaline → disrupted lumen → small infarct → small round lacunae (hole)

Cerebral Venous Occlusion

- Confined to certain patients: pregnancy, post-partum, diabetes mellitus

Head Trauma

Types of Injury

- Effects of head trauma:
 - Direct trauma (eg under skull fracture)
 - Cerebral contusion (local or contracoup)
 - Shearing: diffuse axonal injury → petechial haemorrhage in midbrain, corpus callosum and cerebrum
 - Cerebral swelling
 - Intracranial haemorrhage: epidural, subdural, subarachnoid, intracerebral
 - Concussion: no absolute definition but period of loss of consciousness and anterograde or retrograde amnesia
- Types of skull fracture:
 - Simple: linear or vault
 - Depressed
 - Compound: open to skin or sinuses
 - Skull base → rhinorrhoea or otorrhoea
- Principal injuries from acceleration/deceleration injury:
 - Contusion: coup and contracoup
 - Subdural haematoma from ruptured bridging veins
 - Diffuse axonal injury (shearing injury). Ranges from concussion (very mild, temporary, physiological disturbance) to severe

Assessment

- ABC
- Gross assessment:
 - Localise injury by looking for lumps, depressed fractures, etc
 - CSF from nose or ears ⇒ basal skull fracture
 - Neuro assessment:
 - Use level of consciousness: GCS – best response to verbal, motor and eye response. See Glasgow Coma Scale (GCS), page 481
 - Also pupillary size and exam, limbs
- In diffuse injury the main enemy is ischaemia, which leads to oedema. In localised injury, oedema is the main enemy – acts like a mass lesion
- Presume cervical spine injury until cleared:
 - Need 3 xray views: anterior, lateral and peg (open mouth to view facet joints of C1 and C2, and odontoid peg)
 - Clearance requires clear X-rays AND normal exam. If x-rays clear but tender C spine then CT
- Assess other systems
- Investigations:
 - SXR for minor HI (OK now but were knocked out): mainly for medico legal cover!
 - Cervical spine Xray, even if minor, for occult dens or cervical fracture
 - CT brain if GCS < 15, neuro signs in limbs, cranial nerve palsy or CSF leak
- Criteria for admission, etc:
 - Discharge if GCS 15, low velocity, no seizures or fractures, adequate supervision at home and readmission checklist given to patient
 - Admit if: loss of consciousness/marked post traumatic amnesia or under 5 or over 50
 - CT indicated if GCS < 15 at 4 hours or < 9 at any time, seizures or focal neurological signs
 - Neurosurgical referral if compound head injury or GCS < 15

Raised Intracranial Hypertension (ICP)

- Other causes of ↑intracranial pressure:
 - Bleeding

- Neoplasm
- Brain oedema results from:
 - Inflammatory lesions
 - Infarction
 - Head injury
 - Neoplasms
- Types of brain oedema:
 - Vasogenic cerebral oedema: ↑permeability of cerebral vessels
 - Cytotoxic cerebral oedema: rare. Toxic effect → intracellular oedema
 - If severe acts as a space occupying lesions
- ↑ICP leads to displacement of CSF and compression of veins, then:
 - Herniation of the:
 - Cingulate gyrus under the falx
 - Parahippocampal gyrus past the free edge of the tentorium cerebelli
 - Cerebellar tonsils into the foramen magnum (fatal)
 - And pushing of the midbrain against the tentorium on the opposite side
- Treatment of intracranial hypertension:
 - Aim: Keep ICP low. Principle danger is ↑ICP → ischaemia, transtentorial herniation (uncus of temporal lobe on ipsilateral side) and coning
 - ABC:
 - Maintain airway. If breathing OK then lateral position. 100% O₂
 - Intubate if GCS < 9
 - Aim to keep CPP (Coronary Perfusion Pressure) > 70. CPP = MAP less the greater of ICP or JVP. Coronary blood flow = CPP / CVR (cerebral vascular resistance)
 - In general, keep BP normal:
 - If hypotension then ↓perfusion pressure (bad)
 - Use colloids to maintain BP at 120 – 160 systolic (don't over-hydrate, especially infants)
 - Diuretic: frusemide 40 mg iv
 - Tilt head up → ↑venous return → ↓venous pressure → ↑perfusion pressure
 - ↓O₂ requirements by sedation (Propofol or barbiturates eg thiopentone) and cooling
 - Hyperventilate → reduce CO₂ to 30 – 35 mmHg → ↓cerebral blood flow → ↓cerebral blood volume → ↓brain volume → ↓ICP (but only for short term otherwise ischaemia)
 - Cushing's Reflex (bradycardia, ↑↑hypertension) kicks in when O₂ falls below 20 mls/100g/min
 - Mannitol 0.5 – 1g/kg over 20 mins iv if life threatening – draws fluid from brain, but also a diuretic, so watch for hypotension
 - Drain fluid from ventricle if severe
 - Evacuation of intra-cerebral bleeds
 - Seizures: Clonazepam 0.25 mg/min up to 1 mg plus loading dose of phenytoin
 - Nutrition, urine and bowel management
 - Steroids not effective after head injury

Coma and Stupor

- Checking eyes:
 - Doll's Eye: do eyes remain fixed on target when head is turned. Tests inputs from the neck muscles. Requires linking via medial longitudinal fasciculus of nerves 3, 4, and 6 on both sides
 - Vestibulo-Ocular reflexes: caloric response. 1 ml of ice water evokes nystagmus beating to the opposite side in a normal person. If unconscious, see only deviation without corrective nystagmus
 - In deepening diffuse coma without structural damage, the Dolls eye disappears, then the Caloric response. If pupils still reactive then no coning

Due to Structural damage

- Only if affecting brain areas required to maintain consciousness: usually infarct, bleed or inflammation
- Reticular Activating System: periventricular grey matter from mid pons up, including the hypothalamus and deep grey matter of both hemispheres
- Most supra-tentorial lesions produce coma due to oedema → compression of deep hemispheric structures (paramedian diencephalon)
- Features of coning:
 - Transtentorial: progressive drowsiness followed by pupil changes

- If unilateral cerebral swelling then stretching of ipsilateral 3rd nerve → ↓parasympathetic innervation
- If diffuse bilateral swelling involving brain stem then impairment of both sympathetic and parasympathetic → mid position, irregular pupils
- Posterior fossa coning: headache, stiff neck, ↑BP, ↓pulse

Due to Diffuse depression of brain function

- Usually metabolic encephalopathy
- Key differential from structural damage: Pupillary reflexes retained
- Features: clouded consciousness, difficulty concentrating, altered sleep wake patterns
- Two basic types:
 - Delirium or acute toxic psychosis: agitated, hallucinatory, severely disorientated
 - Acute confusional state: quieter than delirium
- Immediate evaluation: Glucose, thiamine, Na, Ca, Creatinine, pH, PO₂, PCO₂, lumbar puncture, sepsis (septicaemia, lung, urinary tract, meningitis)
- Later: LFT, Sedatives, Blood and CSF culture, Electrolytes and Mg, Coagulation, EEG (absence status)
- Outcome:
 - Sedative drug poisoning: equivalent to GA and will recover with treatment
 - Other medical causes: depends on cause, severity and extent. Only 15% make a good recovery if in coma for more than a few hours
 - Traumatic: better outlook, related to age, 50% die (many instantly), if ophthalmologic signs of brain stem dysfunction then 90% die or remain vegetative

Syncope (Fainting)

- Temporary loss of consciousness (ie up to a minute or so)
- In physically or emotionally stressful situations (eg sight of blood), going out with new partner or boss
- Vasodilation from alcohol, warmth or drugs may contribute
- Usually standing or sitting
- Often groggy and unwell afterwards
- Myoclonus common (seizure like movements, vocalisations): only 10% motionless
- Due to ↓ cerebral blood flow:
 - Postural Hypotension
 - ↓Cardiac output: arrhythmia, VT, periods of asystole (Stokes Adam disease)
- NOT due to: TIA, hypoglycaemia, alcohol. These take longer to recover

Abnormal Speech

- Types:
 - Dysphonia/dysarthria: problems with the mechanics, not ideas, of speech production (eg nerves involved in motor control, connective tissue disease, etc). Say ‘baby hippopotamus’
 - Broca’s (expressive) dysphagia: Non-fluent speech with malformed words. Reading and writing are impaired but comprehension intact. Patients understand questions. Inferio-lateral frontal lesion
 - Wernicke’s (receptive) dysphasia: Empty fluent speech. Maybe mistaken for psychotic speech. Reading writing and comprehension are impaired. Posterior Superior temporal lobe lesion.
 - Cerebellar disease: ataxia of the muscles of speech → slurred and irregular speech
 - Pseudo-bulbar palsy: UMN. Exaggerated jaw jerk, difficulty swallowing, maybe emotional liability. Due to upper motor neuron lesion above the mid pons due to bilateral CV disease, severe MS or motor neuron disease
 - Bulbar palsy: LMN eg facial nerve, Guillain Barre, etc
- Assessment:
 - If speech fluent, grammatical and meaningful or patient can repeat a sentence ⇒ dysphagia unlikely
 - If the patient can comprehend simple instructions with several steps ⇒ Wernicke’s unlikely

Parkinson’s Disease

- Bradykinesia, tremour (70% of cases) and rigidity (unilateral onset) but no early difficulty with gait
- Also lack of arm swing (usually only one side at outset), lack of facial expression, paucity of movement. 30% become demented (either due to Alzheimer’s or widespread Lewy bodies). Also postural hypotension

- Gradual progression and prolonged course
- Pathology:
 - Gross: Pallor of substantia nigra
 - Micro: ↓ in melanin-containing dopaminergic neurones with secondary reactive gliosis. Lewy Bodies may be present in remaining neurones (eosinophilic intracytoplasmic inclusions).
- Treatment:
 - L-Dopa → dyskinesias, and on-off effects after 3 – 5 years. The mainstay of treatment. Give minimum dose to control symptoms, not necessarily signs
 - Carbidopa: prevents peripheral conversion of L-Dopa
 - For younger patients, begin with a dopamine agonist (bromocriptine, pergolide)
 - Selegiline, a MAOB inhibitor delays the time needed for the subsequent introduction of L-Dopa
 - Anticholinergics: stop ACh induced hyper-reactivity: but dry mouth, urinary retention, blurred vision
- Other causes of Parkinsonism. Parkinson Disease is a disease of exclusion:
 - Drug induced parkinsonism eg phenothiazines including antiemetics (eg Maxolon)
 - Multisystem atrophy: also have cerebellar ataxia, eye movement disorder, autonomic dysfunction and pyramidal signs
 - Huntington's Disease: early presentation may mimic Parkinson's, rather than a movement disorder with chorea, myoclonus and dystonia
 - Wilson's Disease: consider in younger patients. Behaviour disturbance, dystonia, flapping tremour. Rare but treatable
 - Diffuse Lewy Body Dementia: Males 2:1. All demented eventually. Most have rigidity, bradykinesia but tremour uncommon. Usually begins with cognitive impairment. See Dementia, page 439

Dystonias

- Most dystonias are caused by basal ganglia disturbance
- Blephrospasm
 - Causes eyes to close all the time, especially in light, wind, etc
 - Tx: inject botulinum toxin
- Hemifacial spasm
- Cervical dystonia: neck turning, head back, etc

Demyelinating Disease

- = Selective, primary destruction of myelin
- Diseases of CNS and PNS myelin do not affect the other
- CNS Demyelinating disease:
 - Multiple Sclerosis
 - Acute Disseminated Encephalomyelitis
 - Progressive Multifocal Leucoencephalopathy (PML)
 - Toxins
 - Leucodystrophies
- PNS Demyelinating Diseases:
 - Guillain-Barre Syndrome
 - Diphtheria
 - Diabetes Mellitus
 - IgM Paraproteinemia
 - Leucodystrophies
 - Hypertrophic neuropathies (eg Charcot-Marie Tooth Disease)
- Secondary Demyelination:
 - Infarction
 - Abscess
 - Contusion/Compression

Multiple Sclerosis

- Chronic autoimmune demyelination of CNS neurons
- Epidemiology:
 - Female to male = 2: 1
 - Peak age of onset 20 to 40 years

- Marked racial difference in susceptibility. Caucasian most common. Africans/Asians rare
- Genetic risk modified by environmental risks up to age 15 (from studies of immigrants)
- Risk 15 times higher if first degree relative with MS. Associated with HLA-DR2 haplotype
- Can be sensory or motor
- Diagnosis: Two lesions in different places at different times. Lesions normally visible on MRI
- One spinal chord lesion may account for diffuse symptoms. As it grows through a spinal chord column a single lesion may progressively affect other areas
- Highly variable course. Relapsing and remitting
- Worse after exercise
- Pathology:
 - Autoimmune destruction of oligodendrocytes, ?triggered by a viral infection in a genetically susceptible host
 - Multiple plaques distributed throughout the cerebral hemispheres (especially periventricular white matter), optic fibres, brain stem, cerebellum and spinal chord
 - Active plaques: are soft yellow or pink and granular. Myelin breakdown → foamy macrophages, T-suppressor cytotoxic cells, T-helper cells, and plasma cell infiltrate. Also reactive astrocytes
 - Chronic plaques: well defined, sclerotic and grey. Sharply defined areas of demyelination with compacted astrocytes processes (⇒ gliosis)
 - Lesions expand by concentric outward growth. Poor correlation between number of plaques and symptoms
- Tx: β -interferons

Progressive Multifocal Leukoencephalopathy (PML)

- Like MS: multiple discrete foci of myelin destruction with relative preservation of axons
- Caused by JC virus (DNA papovavirus common in the community) in immunodeficient patients
- Relentlessly progressive
- Pathology: multiple lipid laden macrophages, oligodendrocytes with ground-glass nuclei (viral inclusions)

Other CNS Degenerative Diseases

Amyotrophic Lateral Sclerosis (ALS)

- Most common form for progressive Motor Neurone Disease
- Affects upper motor neurones (ie layer five of the motor cortex) and lower motor neurones (anterior horn cells)
- 1 – 3 per 100,000 per year
- 5 – 10% autosomal dominant, rest sporadic
- Cause unknown
- Clinical presentation:
 - Lower motor neurons: fasciculations, progressive wasting of muscles, bulbar involvement → difficulty chewing etc, weakness of respiratory muscles
 - Upper motor neurons: spasticity, muscle stiffness, hyperreflexia
 - Sensory, bowel, bladder, ocular movements and cognitive functions relatively preserved
 - Median survival 3 years
- Pathology:
 - Neurons shrink and accumulate lipofuscin
 - No macrophage or inflammatory response
 - Disappearance of axons in Corticospinal and corticobulbar tracts → astrogliosis → lateral sclerosis

Epilepsy

- See Seizures, page 625 for Epilepsy in Childhood, Benign Febrile Convulsions and Anoxic Seizures
- 1:200
- Onset after age 20 ⇒ 10% chance of tumour
- Symptoms:
 - Abrupt onset, brief duration, rapid recovery, and stereotypical recurrence
 - Not just fits: focal signs depending on where in the brain it arises
 - Very long list of differentials to epileptic seizure: See Other Spells, page 136

- Is it epileptiform:
 - Pseudo-seizure (or Non-Epileptic Seizure): either factitious disorder (are deliberately faking) or conversion disorder (they think it's real) (See Somatoform Disorders, page 439)
 - Hard to differentiate: going blue, frothing at mouth and incontinence can happen in pseudo-seizure. Epiletics may not have post-ictal phase
 - Gold standard is EEG: but can't do this in A&E. Fall back is checking whether the person is in any way aware (then it can't be generalised) – eg localising to pain (sternal rub, squeeze thumb nail), drop their hand onto their face
 - Check history: evidence of brain injury, infection, on anticonvulsant meds
 - Pseudo seizure more common in women (10:1) and those with a medical connection (eg doctor/nurse in family, someone with epilepsy)
- Epileptic seizures happen more if: tired, ill, fever, stressed, not taking medication (but these are not classified as 'provoked' as they wouldn't provoke a seizure in a normal person)

Seizure Types

- Generalised: bilaterally symmetrical without local onset
 - Tonic-clonic (Grand mal) seizures: Tonic phase: 10 – 20 secs – extension phase then tremour begins – repetitive relaxation of tonic contraction. Clonic phase: usually 30 seconds, random movements, tongue often bitten
 - Absence (Petit Mal) Seizures: Characteristic type of absence attack. Childhood or adolescent onset, associated with 3/sec spike and wave on the EEG. Blank stare and unresponsive for 5 – 15 seconds. No post-ictal confusion or sleepiness. May also have automatisms and mild clonic motion (usually eyelids at 3 Hz). May be induced by hyperventilation. 80% have no further seizures after 20 years old. Can also have atypical absence seizures. Treat with ethosuximide or sodium valproate
 - Atonic: complete, sudden loss of tone – completely collapse, may injure themselves
 - Tonic: sustained contraction, maybe with fine tremour
 - Myoclonic: Sudden, very brief jerk but still generalised
 - Clonic: rhythmic jerking
 - Infantile spasms:
 - Sudden bilateral symmetrical jerk, extensor or flexor. Can be subtle, come in clusters
 - Usually around 3 – 6 months, boys > girls
 - Grow out of the spasms
 - Bad prognosis: cerebral palsy, retardation, etc
 - Medical emergency: try to urgently get them under control
- Partial: Begin locally
 - In simple partial seizures consciousness is preserved.
 - Complex partial seizures are focal seizures in which consciousness is altered (eg blank unresponsiveness followed by automatisms, eg lip smacking, other semipurposeful activity) – usually temporal lobe but may be frontal. Can go on for minutes. Aware it is coming (cf absence which is sudden)
 - Partial seizure secondarily generalised: they have an awareness first
 - Localising it:
 - Preceding aura: olfactory, visceral, auditory, visual, *déjà vu*
 - Dystonic posturing: contraction of agonist and antagonist muscles
 - Post-ictal Todd's Syndrome: if they have one area of weakness after a seizures (ie one hand weaker than the other) then it started locally
- Automatic behaviour usually seen in complex partial seizures: but can be in absence (petit mal) seizures. Eg Oral or manual automatisms
- Seizure location:
 - Frontal: focal tonic or clonic motor activity, posturing, prominent motor automatisms but no orofacial or experiential automatisms
 - Central: focal clonic seizures with preservation of awareness
 - Temporal: experiential, gustatory or olfactory hallucination. Motion arrest, automatisms
 - Parietal: exclusively somatosensory manifestations
 - Posterior: polymodal sensory, visual, auditory or somatosensory hallucinations
- Sorting out type of seizure:
 - When do the seizures occur
 - Does patient know they're going to have a seizure

- What can the patient recall
- Detailed description from observers:
 - Are they aware – will they respond
 - Are their automatisms
 - Is there dystonic posturing
 - How long did it last
- After the seizure: are they confused, can they speak, any post-ictal Todd's

Treatment

- Diagnosis is clinical. EEG helps with severity, classification, to localise a surgically remediable abnormality (eg hippocampal sclerosis), and to differentiate pseudo-seizures
- Don't treat until you're sure it's epilepsy
- Anticonvulsants suppress seizure activity in 80%
- Principles of drug treatment:
 - When to treat: often wait for second seizure – although treatment after the first → ↓ occurrence, but no long term change in outcome
 - Use only one drug
 - Tailor drug to seizure type
 - Introduce slowly. Takes about 5 days to stabilise a change in dose
 - Monitor drug level: for other than phenytoin, this is to check compliance. Beware – plasma level at which seizure control is obtained is variable
 - Consider withdrawal of drugs after 2 years without seizure, slowly over 6 months
- Mode of action unknown – but may ↓GABA breakdown, as well as modifying flux of Na, K and Ca ions
- Usual drugs:
 - Idiot's guide: carbamazepine for partial seizures and Valproate for generalised

	Seizure type	Examples of conventional drugs
Partial Seizures	Simple partial, Complex partial and Partial secondarily generalised	Carbamazepine (<i>Tegretol</i>), Phenytoin, Sodium Valproate (<i>Epilim</i>), Penobarbitone, Primidone
Generalised seizures	Absence	Clonazepam (a BZD), Ethosuximide, Valproate
	Myoclonic	Valproate
	Tonic-clonic	Carbamazepine, Phenytoin, Valproate, Penobarbitone, Primidone

- Conventional drugs have hepatic clearance
- Side Effects:
 - General lethargy, ↓concentration, unsteadiness, dizziness
 - ↑LFTs: but serious hepatotoxicity rare. Especially Valproate
 - Rarely bone marrow suppression
 - Pregnancy:
 - Epilepsy often worsens during pregnancy
 - Plasma concentration of drugs falls due to pharmacokinetic changes and ↓compliance
 - Teratogenic: 3% risk of malformation on 1 drug (also, epilepsy itself can be teratogenic - ?hypoxia during seizure)
 - % in breast milk varies by drug
 - Specific drugs:
 - Carbamazepine: enzyme inducer
 - Phenytoin: Dose-dependent kinetics → small ↑ in dose may → ↑↑ in plasma concentration, SE: ataxia, peripheral neuropathy, gingivitis
- Must be seizure free (with or without treatment) for 12 months before you can drive. Obliged to tell LTSA on diagnosis if the patient won't and continues to drive

Status Epilepticus

- Repeated seizures without regaining consciousness
- No one knows how long is too long: but after 10 minutes ↑risk of damage

- If not sure whether it's epileptiform then must still treat for status
- Treatment:
 - Protect and maintain airway, insert oral airway
 - Prevent injury
 - 100% oxygen
 - Diazepam 10 – 20 mgs iv, not exceeding 2 – 5 mgs per minute. If no iv access give rectally with 10 – 20 ml normal saline. Duration is brief and another anticonvulsant is required. Avoid repeating diazepam → cardiorespiratory collapse. If no response give clonazepam 1 – 4 mg iv
 - Phenytoin 50 mg/min iv (25 mg/min in cardiovascular disease), usual adult dose 1250 mg in 100 mls saline over no more than 20 minutes. Monitor BP and heart rate
 - If established, give phenobarbitone
 - If refractory, then anaesthesia with propofol or thiopentone. Taper after 12 – 24 hours

Other Spells

- Commonly misdiagnosed as seizures
- Paroxysmal non-epileptic events without altered consciousness: Jitteriness, migraine with focal aura, hyperventilation, acute paroxysmal vertigo, shuddering attacks, anxiety states (eg panic attack), psychosis, drug induced dystonias, masturbation, tics, etc
- Paroxysmal non-epileptic events with altered consciousness: Day dreaming, breath holding spells, reflex syncope, TIAs, psychosis, pseudo-seizures, delirium, metabolic disorders, other brain insult (infection, haemorrhage), ritualistic movements, migraine, arrhythmias, drugs substance abuse
- Paroxysmal non-epileptic events related to sleep: benign sleep myoclonus of infancy, head banging, night terrors, hypnagogic jerks, sleep walking, sleep apnoea

Brain Tumours

Epidemiology

- 2% of all cancer deaths
- 20% of paediatric neoplasms (21 per 100,000 at 2 years)
- Incidence 8 – 10 per 100,000 per year
- Incidence lowest in teens rises to 16 per 100,000 in 70's

Histology

- Cell types in the brain: neurons, microglia (lymphocytic derived, phagocytic function), oligodendrocyte (myelination), choroid cells (make CSF), astrocytes (structural support, star shaped, multiply in sites of injury), ependymal cells (line ventricles), meninges, pituitary, lipophages (histiocytes which phagocytose lipid rich myelin – non-specific marker of white matter destruction)
- Neuropil = intercellular matrix in the CNS – tangled processes of neurones, astrocytes, oligodendrocytes
- Tumour → vasogenic oedema
- Incidence of neoplasms:
 - Neuroepithelial (ie intrinsic brain cells) → Gliomas: 52%
 - Astrocytoma: 44%. When severe = Glial Blastoma Multiforme (GBM)
 - Ependymoma 3%
 - Oligodendrioglioma: 2%
 - Medulloblastoma: 3%
 - Metastatic 15% (eg breast, lung)
 - Meningioma: 15%
 - Pituitary: 8%
 - Vestibular Schwannoma: 8%
 - Also retinoblastoma
- Different incidence in children:
 - Normally posterior fossa (as opposed to anterior fossa in adults) and different frequencies of different types
 - Most common tumours are pilocytic astrocytoma and medulloblastoma

Astrocytoma

- Locally invasive

- Presentation:
 - ↑ICP from obstructive hydrocephalus and from space occupying lesion
 - Focal neurological deficit
 - Epilepsy: ¾ of high grade astrocytoma present with seizure
 - Endocrine
- By age:
 - Cerebral hemispheres in middle and old age
 - Spinal cord in young adults
 - Cerebellum and pons in childhood
- Pathology:
 - Benign = won't recur if removed. However, also need to be accessible to have a good prognosis
 - Heterogeneous – range from well-differentiated to anaplastic
 - Characteristic fibrillary background of cytoplasmic processes containing Glial Fibrillary Acidic Protein (GFAP). Can use immunohistochemistry to stain for these. May congregate to form Rosenthal fibres
 - Graded from 1 (low grade, and hard to differentiate from reactive gliosis although these rarely produce a distinct mass) to 3 (anaplastic) to 4 (glioblastoma multiforme – GBM, mitoses common compared with low grade, pallisading necrosis differentiates it from grade 3). Low grade have a tendency to become high grade and are also hard to cure due to their infiltrative nature
 - Grossly: Infiltrative. Either firm or soft/gelatinous. GBM is heterogeneous with focal haemorrhage and necrosis
 - Pilocytic variant of astrocytoma: most common astrocytoma of *childhood*. Excellent prognosis. Cystic. Usually in cerebellum
 - Astrocytomas (grade 3 or 4) are the most common gliomas to arise subsequent to radiotherapy (usually 5 – 25 years later)
- Investigations: CT and MRI. Xray and angiography obsolete
- Management:
 - Dexamethasone: ↓vasogenic oedema → ↓ ICP
 - Anticonvulsants → ↓seizures
 - MR spectroscopy → biopsy by framed stereotactic or image guidance
 - Surgery: debulking or macroscopic excision (only if not deep or eloquent areas otherwise too much damage from surgery – use radiotherapy for these)
 - Arguments for macroscopic excision. High-grade gliomas weigh 100g at diagnosis = 10E11 cells. After macroscopic excision will still have 10E10 cells. Effective radiotherapy → 10E8 cells. Chemo/radio therapy only kills cells in division

Prognosis

- For GBM: Median survival:
 - Without surgery, 17 wks
 - With surgery, radio and chemo, 51 wks
- For low grade glioma: 50% 5 year survival if total macro excision

Other Neuroepithelial Tumours

- Subependymal giant cell astrocytoma: associated with tuberous sclerosis
- Neuronal tumours: not common. Include:
 - Gangliocytomas
 - Gangliogliomas: better prognosis
 - Cerebral neuroblastoma: Rare, in children. Resemble peripheral neuroblastomas – ‘small round blue-cell tumours’
- Oligodendrogloma:
 - 5 – 15% of gliomas
 - Radiographically, well demarcated and often show calcification (key differential)
 - Grossly: gelatinous masses +/- cysts and/or haemorrhage
- Ependymoma: usually in fourth ventricle → outflow obstruction. Also in intramedullary portions of the spinal chord. Slow growing and not malignant but poor prognosis. CSF spread is common. Significant histological features: ‘true’ rosette and perivascular pseudo-rosette. Numerous subtypes
- Choroid Plexus Papilloma: rare. In ventricles. Usually children. Cauliflower type projections into ventricular lumen

- Pineal Neoplasia: Intrinsic tumours are Pineocytoma and Pineoblastoma. Germ cell tumours are the most common, including choriocarcinoma, teratoma, etc. Present with mass effects in men aged 20 – 40. Differential: lymphoma or metastatic cancer
- Hemangioblastoma: Highly vascularised, cystic tumours, mainly in the cerebellar hemispheres
- Craniopharyngioma: Arise from the epithelium of Rathke's pouch – part of the embryonic nasopharynx which forms the anterior lobe of the pituitary. Present due to mass effects in children and adolescents. Histology: see keratin pearls.
- Primitive Neuroectodermal Tumours (PNETS):
 - Rare tumours in children arising from primitive glial or neuronal precursor cells. Aggressive and poor prognosis. Usually “small round blue-cell tumour” (differential includes lymphoma)
 - Medulloblastoma: a distinctive PNET. Occurs exclusively in the cerebellum, mainly in children, mainly as a midline mass. Cause CSF obstruction and spread via CSF
- Schwannoma: In the cranial vault, nearly all schwannomas are attached to the 8th cranial nerve in the cerebellar pontine angle ⇒ acoustic neuroma
- Lymphoma: Either originated in the CNS or from systemic invasion (usually affect the meninges). Usually B-cell lymphomas

Pituitary

- Pituitary Adenoma: benign neoplasm in anterior lobe of the pituitary
 - Present with either mass effects (including on the rest of the pituitary) and excess hormone secretion
 - At any age or sex, but most common in men aged 20 – 50
 - Classified on the basis of hormones they secrete by immunocytochemistry. Poor correlation between acidophils, basophils and chromophobes and the hormones secreted
- Carcinomas are rare. Diagnosis requires gross brain invasion or discontinuous spread

Metastatic Brain Tumours

- 20% have intracranial mets at autopsy
- In 15% primary organ not found
- Surgery for solitary met if primary site controlled or for symptomatic control or for diagnosis
- Most mets are carcinomas. 80% are due to (in decreasing frequency): lung, breast, skin (melanoma), kidney and GI
- Prognosis:
 - Melanoma & lung solitary: < 30% 1 year survival
 - Breast solitary: 50%
 - Undetermined solitary: 50%

Meningioma

- 20% of primary intracranial neoplasms
- Incidence peaks in females aged 40 - 50
- Benign in 90 – 95%
- Occur anywhere round brain
- Well circumscribed → mass effects
- Histology: meningothelial whorls and psammoma bodies
- Tx: surgical excision

Spinal Chord Syndromes

- Prognosis depends on time to treatment: speed is important
- Trauma:
 - Transfer to specialist unit within 24 hours unless medically unstable
 - Catheterise: bladder won't work → urinary retention
 - Check underneath them before transferring. An unfeared pen or other object will cause a full thickness pressure sore during 2 hour transfer → 3 months to heal
 - 200 per year in NZ (same as severe HI). Mainly young men → long term disability, lots of ongoing psychological problems
- Extradural spinal cord compression (EDSCC)
 - Usually cancer. Also haemorrhage (epidural haematoma) or epidural abscess
 - Key questions: where is the lesion, what is the lesion (eg weight loss, past cancer history ⇒ cancer)

- If there is a clear level below which these is sensory abnormality \Rightarrow spinal chord
- If both legs then spinal chord (usually). Can be parasagittal meningioma (very rare)
- Are arms normal: if so T2 highest possible level
- If there are signs of an upper motor neuron lesion in the legs then it MUST be above the cell bodies of L3 – S5 in the conus of the spinal chord, which is at T12 vertebral level \Rightarrow if UMN lesion then it is in thoracic spine or above
- 95% have pain at the site of compression \rightarrow very good indicator. Tap gently down spinal chord with tendon hammer
- Imaging: MRI
- If can't be completely sure it's cancer MUST biopsy (eg chronic infection)
- Cancers:
 - Lymphoma
 - Female: breast
 - Male: lung, sometimes prostate
- Transverse Myelitis:
 - Inflammation of spinal chord itself
 - Same symptoms as EDSCC, but no compressing signs on MRI (usually normal – NO mass lesion)
 - Usually due to a demyelinating type inflammation – can be due to MS (= 2 demyelinating lesions in the CNS at different times and different places)
 - Could also be sarcoidosis \rightarrow granulomas and inflammation (very rare to only occur in spinal chord)
- Corda Equina Syndrome (CES)
 - Triad: leg weakness, sensory loss, sphincter problems (usually overflow not urgency – ie LMN)
 - Classic description: ‘saddle anaesthesia’ – anaesthesia in sacral dermatomes – eg feels like cotton wool when sitting on the toilet seat. May be only symptom. Usually bilateral
 - If due to central disc prolapse can be fixed if treated urgently \Rightarrow medical emergency
 - 95% of disc prolapses are at L4/L5 or L5/S1: but most are laterally into nerve root, not central into cauda equina
- Acute Inflammatory Demyelinating Polyradiculopathy (AIDP)
 - = Guillain-Barre
 - = Demyelination of multiple peripheral nerves
 - Symptoms: ascending paralysis. Affects arms, legs and respiratory. Only a portion will get to ventilatory arrest, but can deteriorate very quickly \Rightarrow test FEV1 4 hourly while normal (normal > 4 l), to ICU if < 2 l. (O₂ saturation and PO₂ won't tell you till too late)
 - Predominantly motor problem: unlikely to be AIDP if lots of sensory symptoms
 - Signs: LMN and arreflexia (arreflexia is a classic sign)
 - Tests:
 - Lumbar puncture: ↑protein but no ↑WBC
 - Nerve conduction studies: motor conduction < 30 m/sec (normal > 40 – 50 m/sec)
 - Treatment: IV γ globulin and plasmaphoresis (plasma exchange). Heparin to prevent PE
 - Not related to Chronic Inflammatory Demyelinating Polyradiculopathy

Headaches

- See also Headaches, page 624 for Headaches in Children
- Recent onset of severe headache: the most common cause is idiopathic
- Ask about associations/antecedents
- Red flags: fever, change in mental status/personality, fits, focal neurological signs, sudden and severe, affected by postural change, normally headache free, waking at night or in the morning with a headache
- Types of headache:
 - Tension headaches, eg chronic daily headache, gradual onset (chronic), sleep not disturbed, treat by ↓stress (massage, relaxation). ? Depression. Types: post-coital, ergotamine misuse
 - Cluster headache: clusters of extreme, recurrent *non*-throbbing deep pain in and around an eye, spreading onto the face. Eye typically becomes swollen and watery
 - Migraine: visual symptoms, unilateral, throbbing, nausea, aura
 - Facial structure: eg TMJ dysfunction, sinusitis, NOT teeth
 - Neuralgic: eg idiopathic, trigeminal neuralgia
 - ‘True vascular headache’: associated with TIA/stroke, artery dissection, giant cell arteritis
 - Associated with ↑ICP: focal lesions, venous thrombosis, meningitis, severe hypertension

- Acute: ?meningitis, sinusitis, head injury
- Associated with post Lumbar puncture
- Treatment: Ongoing unchanged tension or migraine headache: TCAs
- Differential of morning headache:
 - ↑ICP
 - ↑CO₂ (eg sleep apnoea)
 - Diabetic going hypoglycaemic overnight

Myasthenia Gravis

- Antibodies to Ach receptors → weakness, fatigues with repetition
- Affects eye movement in 15%
- Treatment:
 - Immunosuppressives: Prednisone, azathioprine, cyclosporin
 - Take out thymus – many have hyperplasia or thymoma
- Myasthenia Gravis Crisis:
 - Triggers: Respiratory infection, change in medication
 - → Respiratory failure due to weakness, can be insidious
 - Consider ICU admission and ventilation

Other neurological emergencies

- Meningococcal meningitis. See Infections of the CNS, page 495.
- Encephalitis: fever, stiff neck, strange behaviour, unable to make new memories, seizures. Acyclovir 10 mg/kg 8 hourly (> 20% caused by Herpes Simplex)
- Temporal arteritis/Giant Cell Arteritis: See Giant Cell arteritis/Temporal Arteritis, page 282

Other

- Trigeminal neuralgia: momentary severe shooting pain in one division of 5th nerve due to touching, chewing or speaking. Responds to Tegretol
- Locked-in syndrome: pontine infarction → quadriplegia and variable loss of all reflex and horizontal eye movements. Vertical eye movement or eyelid movement may be the only means of communication
- Cerebellar infarction/haemorrhage: vertigo, headache, and abnormalities of eye movements (eg saccadic deficits). May lead to life threatening compression/coning of the brainstem

Eyes

History

- Common presenting complaints:
 - Loss of vision: blurred, double, distorted, field loss, glare, colour defect
 - Disturbance of sensation: pain, itching, photophobia. If sharp pain → surface, if throbbing pain → deeper lesion
 - Changes in appearance: red and/or discharge
- Associated symptoms
- Past ocular history: trauma, surgery, spectacles
- General medical history: diabetes, allergy, medications
- Family History: squint, glaucoma, refractive error
- Social History: Assess impact on function (eg work, hobbies, support, dependents). Also smoking → ↑incidence of cataract

Physical Examination

- Trying to work out where is the problem: refractive, obstruction of light through the transparent tissues of the eye, or neural problem
- Measure Visual Acuity:
 - One at a time. Wear glasses
 - Snellen's Chart: Distance of chart (normally 6 metres)/Distance they could read. Smaller fraction is worse
 - If can't see chart at all, then Count Fingers (CF) at X metres
 - If can't count fingers then Perceive Light (PL): flash torch on and off in eyes – can they see it

- Check with pinhole, if clearer \Rightarrow refractive error or corneal scarring, refer to optometrist. If worse \Rightarrow retinal pathology
- Also check visual fields, colour, stereo vision
- External inspection:
 - Be systematic: look for changes in shape, size, position, colour, transparency, is it focal or diffuse
 - Pupil reflexes: Should be simultaneous *and* equal. Swinging light test: Alternate light from one eye to the other, swapping it quickly. Both pupils should stay the same. Sensitive and complete test of neural pathways. If this shows a problem, test for an efferent pupillary defect with the near reflex test
- Internal inspection with ophthalmoscope:
 - Get patient to look at target a long way away: relaxes accommodation. Dim the light \rightarrow dilation
 - Dilate pupil with Madriasil (not atropine, T $\frac{1}{2}$ too long)
 - Check for:
 - Red reflex defects: eg cataract, intra-ocular blood
 - Reduced transparency (compare two eyes)
 - Cup and disk:
 - Disk is 15 degrees nasal to fixation. To examine macula, get patient to look directly at the light
 - Check disk for distinct margins and symmetry
 - Physiology cup is blood vessels in the centre of the nerve – not nerves
 - Normal cup to disc ratio $< 1/3$ (but lots of variation). Check it's the same in both eyes
 - Large and/or deep cup sign of glaucoma (vessels ‘diving into’ the cup) – especially if eyes different. Large ratio
 - Papilloedema: non-inflammatory nerve oedema due optic nerve axon flow obstruction or \uparrow ICP \rightarrow red disk swelling towards you, blurred margins of disk but no early visual loss. Venous obstruction may \rightarrow haemorrhage. If bilateral then \uparrow ICP
 - Papillitis: optic nerve head inflammation \rightarrow swollen disk with visual loss. If unilateral then optic neuritis (\downarrow colour vision, orbital pain), sarcoidosis, Tb, Syphilis, etc
 - Pseudopapilloedema: occurs in hypermetropia, disc is smaller than normal and crowded
 - Fundus pathology: maculopathy, optic neuropathy, retinal detachment
 - Refractive errors: hard to focus on retina
 - Arteries: narrow, bright red, wavy. Veins: thicker, straight
 - Amount of melanin in choroid layer \rightarrow variation in pigmentation of retina. Deep green patch = coronal nevus (benign)
 - Clinical usefulness depends on good instrument, good technique, knowledge of normal anatomy and normal variations

Anatomy

- Fovea: dip in middle of retina. Only photoreceptors, neural connections heaped up around it
- Macula: ill defined area around fovea
- Uvea = iris, ciliary body and choroid. Iritis = anterior uveitis
- Reflex pathway: retina \rightarrow optic nerve \rightarrow optic chiasm \rightarrow optic tract \rightarrow lateral geniculate nuclei \rightarrow optic radiation and brain stem \rightarrow Edinger Westphal nucleus \rightarrow 3rd nerve

Loss of Vision

- Is it bilateral or unilateral?
- Sudden: Woke up with it \Rightarrow Vascular: Central retinal artery or vein occlusion, ischaemic optic neuropathy, vitreous haemorrhage, CVA, preretinal haemorrhage
- Suddenish: Gradual over a few days: Closed angle glaucoma (hours), infection, inflammation, retinal detachment, optic neuritis
- Gradual: Months to Years: Refractive, cataract, primary open angle glaucoma, age related macular degeneration, retinopathy (eg diabetes, hypertension)
- Chronic visual loss:

	Uniocular	Binocular
Cornea & Red Reflex	Keratoconus, cataract, uveitis	Corneal dystrophies, cataract, uveitis
Visual Fields	Retinal detachment, meningioma	Retinitis pigmentosa, pituitary lesions
Pupils and IOP	Glaucoma	Glaucoma

Dilate for Fundoscopy	Malignant melanoma, optic atrophy	Maculopathies, optic atrophy, papilloedema
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Age Related Macular Degeneration

- Loss of visual acuity with peripheral vision intact
- Observe stippling and depigmentation of macula
- Can be uni or bilateral
- Age-related types:
 - Dry (atrophic) macular degeneration: thinning of macula, gradual. No cure. Atrophy of photoreceptors, loss of outer nuclear layer
 - Wet (exudative) macular degeneration: May be due to Choroidal Neovascular Membranes, unilateral with onset over several weeks. Straight lines appear wavy → refer as laser treatment slows progression
- Symptoms: blurred central vision, distortion of straight lines

Eye Trauma

- Mechanical: blunt/sharp, superficial/penetrating
- Chemical: alkali the worst. Local anaesthetic then irrigate for 30 minutes (less time already irrigated before presentation). If not toxic nor significantly inflamed, if VA OK and no fluorescein staining then chloramphenicol eyedrops qid for 5 days
- Radiation: UV, thermal, arc flash. Comes on hours after exposure, is very painful. Eye is very red, multiple fine specks of fluorescein staining. Usually resolves in 24 hours. Treat as an abrasion (pad both eyes)
- Hyphema: blood in anterior chamber. Refer for opinion but don't normally treat. Check for corneal abrasion, traumatic mydriasis, eye movements, blowout fracture of orbital floor, intra-ocular bleed
- Penetrating Eye Injuries can be missed by subconjunctival bleed. Always refer if at risk. If metal vs. metal, always do an x-ray otherwise blind from Fe toxicity. Also rose thorns. Teardrop shaped cornea is a PEI until proven otherwise. Refer immediately. Lie down, im antiemetic to prevent vomiting. Keep nil-by-mouth
- Distorted pupil: penetrating injury until proven otherwise ⇒ nil by mouth, shield eye, antibiotics, antiemetic, refer
- Foreign bodies: remove with 25-gauge needle and topical anaesthetic drops. Steady fixation of eye is key. Always evert upper eyelid to look for further foreign bodies
- Corneal abrasions: Very painful and photophobic. Stain with fluorescein. Most heal within 24 hours. Refer if abrasion large or central, if cornea hazy, VA reduced or eye is very inflamed. Double pad eye well. Apply chloramphenicol ointment stat and bd for 5 days. Never give anaesthetic drops to take home – can cause ulceration and blindness
- Lid laceration: suture anything not penetrating, or not involving lid margin or tear drainage (refer these)

Retinal Detachment

- Higher risk in near-sighted (myopic)
- Can be caused by blunt trauma
- Due to vitreous shrinkage, tears/holes in retina (eg with age), or underlying pathology
- Symptoms: sudden changes in vision – watery or shadowy patch, sudden ↑ in number of floaters (spots in vision), loss of visual field (like a descending curtain)
- Need rapid treatment: seal tear with laser
- Causes:
 - Exudative detachment: accumulation of fluid under the retina due to leaky vessels, eg tumour, vascular abnormality
 - Traction detachment: vitreous becomes organised following trauma or neovascularisation and pulls on the retina

The Red Eye

- Never use steroids in an undiagnosed red eye (can worsen ulcers, etc)
- Diagnostic Tree:
 - Unilateral:
 - No Pain, vision normal: subconjunctival haemorrhage, episcleritis, pterygium, conjunctivitis
 - Pain and normal vision: if no corneal staining: Anterior uveitis, scleritis, HZO. If corneal scarring: HSV, marginal ulcer

- Pain and vision reduced: If no corneal staining: severe uveitis, angle closure glaucoma, secondary glaucoma. If corneal staining: HSV, Bacterial keratitis, HZO
- Binocular:
 - No pain, good vision: bacterial, viral or allergic conjunctivitis
 - Pain, vision good or poor: viral or chlamydial keratoconjunctivitis
- Subconjunctival bleed: self limiting unless severely hypertensive or coagulopathy
- Conjunctivitis:
 - Initially unilateral, may → bilateral due to cross infection
 - Feeling of surface grittiness
 - Causes:
 - Infective: See Eye Infections, page 144
 - Allergic: eg eczema, allergy to protein deposits on poorly cleaned soft contacts
 - Chemical/mechanical
 - Baby: 1 month with pussy discharge → urgent referral (?blocked and infected lacrimal duct)
 - Never pad a discharging eye
- Blepharitis
 - = Lid inflammation
 - Eyelash 'dandruff'
 - Meibomian gland dysfunction: usually staph infection. 30ish glands under they eyelid normally secrete lipid to cover tear film
 - Clean with saline or bicarbonate solution
- Chalazion: Red nodule in the lid. Due to obstruction and infection of a Meibomian gland. Microscopically granulomatous inflammation (basically a burst sebaceous gland)
- Corneal Ulcer: See HSV infections below.
- Keratitis:
 - Corneal inflammatory disease
 - Symptoms: deeper, aching pain
 - Aetiology: infective, contact lens, staph hypersensitivity, exposure keratopathy (eg 7th nerve palsy)
 - Signs: speckled light reflex ⇒ corneal oedema
- Shingles affecting face: refer within 7 – 10 days to check for intra-ocular complications. Pain is due to trigeminal neuralgia
- Iritis:
 - Frontal headache, photophobia, not watering. Usually unilateral
 - White cells and fibrous exudate in anterior aqueous. May be white cells at bottom of cornea
 - Usually autoimmune: Ankylosing Spondylitis, Crohn's. Treat with steroids, and dilating drops to keep iris mobile
 - Rarely infective (eg Tb)
- Episcleritis:
 - = Localised inflammation of sclera. Treatment: topical NSAIDs
 - Acute onset, mild pain, young adults, usually sectorial, no corneal signs
 - Cf Scleritis: pain, VA decreased, tender, sectorial or diffuse, corneal signs
- Pterygium:
 - Conjunctival overgrowth growing over cornea. Age related changes due to sun exposure
 - Refer if enlarging and vascularised. Differential: squamous cell carcinoma.
 - Pinguecula: White epibulbar nodule similar to pterygium
- Acute Glaucoma: See Primary Closed-angle Glaucoma, page 144

Glaucoma

- Usually due to outflow obstruction: damage to the trabecular meshwork overlying the channel of schlemm → ↑ resistance to flow → ↑ steady state intraocular pressure → ↓vascular perfusion of the neural tissue → blindness
- Classification:
 - Primary:
 - Open angle (chronic)
 - Closed angle (acute)
 - Secondary: eg iritis, trauma, blood in the eye, etc

Primary Open-angle Glaucoma

- Epidemiology:
 - Leading cause of preventable blindness
 - Risk factors: age, near-sightedness, African/Asian ancestry, family history, past eye injury, a history of severe anaemia or shock, steroid medication
 - Most common sort, gradual impairment of aqueous drainage, insidious loss of sight
 - 2% of over 50 years
 - 1 in 7 risk if primary relative has it
- Presentation:
 - Central field defect – arculate shape with macular sparing
 - Cupping of the disk due to ischaemic atrophy of the nerve fibre layer
 - Bullous keratopathy – oedema of the cornea
- Screen with tonometry (measuring intra-ocular pressure), test visual fields.
- Is diagnosed by cupping of the optic disk: not by ↑intra-ocular pressure. 17% of people with glaucoma have ‘normal’ IOP.
- Pathology:
 - ↑Resistance to outflow (pathogenesis not clearly understood) → ↑aqueous humour → ↑intra-ocular pressure (normal is < 22 mmHg)
 - Leads to damage to ganglion nerve cell axon (final output) at the optic nerve head. Due to vascular insufficiency as nerves exit the eye
 - Affects peripheral bundles preferentially: spares papillo-macular bundle
- Treatment: Medication, laser treatment to enlarge the drain (trabeculoplasty)

Primary Closed-angle Glaucoma

- Iris is pushed forward and acutely occludes the trabecular meshwork → ↓drainage
- Rare but vision threatening
- Unilateral, acute visual loss, pain, nausea and vomiting, dilated, non-reactive pupil
- Precipitating factors: long sited (narrow anterior chamber, narrow iridocorneal angle), and when pupil dilated for a long time (dim light)
- Can be congenital
- Once resolved, put hole through iris (iridotomy): no further obstruction possible

Secondary Glaucoma

- Secondary open angle glaucoma: Outflow system is obstructed mechanically by debris (ie gunge up trabecular meshwork). Rare. Eg Haemolytic glaucoma, lens protein glaucoma
- Secondary closed angle glaucoma: Can be due to neovascularisation ‘zipping up’ the angle, secondary to ischaemic eyes (eg diabetes, central retinal vein occlusion)

Eye Infections

- Viral Infections:
 - Adenovirus types 8 (epidemic) and 3 and 7 (sporadic). Conjunctivitis with pre-auricular lymph node hyperplasia. Over about a week get small white spots (WBC accumulations) just below the surface of the cornea
 - HSV:
 - Gives Herpes Simplex Keratitis.
 - Dendritic ulceration with neovascularisation. Chronic inflammation and scarring. May lead to small white vesicles around the eye.
 - Viewed with fluorescein drops under cobalt light (stains where there is no epithelium)
 - Branching pattern ⇒ Herpes Simplex Virus. Never give steroids: → worse infection → permanent damage
- Bacterial: Usually puss. Always bilateral:
 - Standard bacterial conjunctivitis: treatment chloremphenicol eye drops
 - Trachoma: Due to Chlamydia. Commonest cause of blindness in the tropics. Less common than other causes in NZ. Chronic. Suspect if no response to topical antibiotics. Initially the conjunctival epithelium is infected → scarring of the eye lid → abrasion of cornea → over years get panus (fibrovascular layer) over the cornea
 - Gonorrhoea: ↑pre-auricular nodes

Optic Nerve Lesions

- Optic atrophy: pallor of the optic disk, and damage to the retinal nerve layer, optic nerve or tract leading to ↓visual acuity or field loss. Due to neuritis, compression, ischaemia, glaucoma
- Optic Neuritis: Age 18 – 40, more common in women. Pain on movement of eye, with central fog patch, colour desaturation. Worsens over hours to days, may lose sight completely, gradually improves over 4 – 6 weeks. 70% chance of developing MS over 10 years
- Anterior Ischaemic Optic Neuropathy: Sudden painless unilateral visual loss in an older person. Seldom improves. Due to occlusion of the arterioles to the optic nerve head
- Compressive Optic neuropathy: insidious loss of central vision in one eye, especially colour. Usually meningioma of optic nerve

Nerve Lesions Affecting Eye movement

- Droopy lid (ptosis) and small pupil (Horner's syndrome) – due to lesions in the brain stem, in the apex of the lung, in the neck or on the carotid artery (eg carotid dissection)
- Droopy eye lid and large pupil non reactive to light: 3rd nerve palsy – eye turned down and out due to weakness of MR, SR, IO, and IR
- Differential for Ptosis: idiopathic (esp elderly), myasthenia, muscular dystrophies, myotonic dystrophy
- Nystagmus: if present in all directions will be central (commonest cause is antiepileptics)

Retinal Vascular Disease

- Damage to large vessels in the eye
- Occlusion of the central retinal artery:
 - Due to atheroma, thrombus, embolis, arteritis
 - Retina is white and totally infarcted
- Occlusion of the central retinal vein:
 - Haemorrhagic infarction
 - Collateral supply means some vision is recoverable
 - Retina is a mass of red, veins big and tortuous, cotton wool spots

Focal Ischaemic Retinal Disease

- Affects little vessels
- Features:
 - Cotton wool spots:
 - Fluffy and off-white/yellow
 - Due to micro-infarction → superficial area of necrosis and oedema
 - Axons are disrupted and become distended (cytoid bodies)
 - Resolve in 6 weeks
 - Hard exudates:
 - Discrete, brighter white, often around macula
 - Plasma leaks from damaged capillaries (secondary to thickened basement membrane) in the outer plexiform layer (deeper in the retina) and forms proteinaceous lakes
 - Resolves over several months
 - Haemorrhage: usually arises from microemboli/thrombi damaging vessels
 - Flame: a small arteriole bursts into nerve fibre layer and spreads along nerve fibres
 - Dot: capillary bursts into outer plexiform layer
 - Blot: into the subretinal space
 - Roth's spots: central white infarct surrounded by haemorrhage
 - Microaneurysms:
 - Round or oval dilations of capillaries – look like lots of very little red dots
 - Central in diabetes, peripheral in central retinal vein occlusion
 - Due to reduced numbers of pericytes surrounding capillaries
 - Neovascularisation:
 - Response of the eye to vascular insufficiency, secondary to angiogenesis factors from ischaemia: proliferate around the margin of non-perfusion. Detect with fluorescein angiogram
 - Appears as fine lace work of new vessels. They leak and bleed
 - Sites:
 - Iris surface → neovascular glaucoma, ectropion uvea
 - Pupillary membrane → Posterior Synichiae

- Vitreal Surface → haemorrhage, pre-retinal fibrovascular membranes → scarring → retinal detachment
- Easy to see if over optic disk (normally should only be large vessels)

- Differentiating between Hypertensive and diabetic retinopathy:

	Hypertensive Retinopathy	Diabetic Retinopathy
Vessel	Arterioles	Capillaries/veins
Site	Superficial nerve fibre layer	Deep (non-proliferative) Superficial (proliferative)
Pathology	Medial hypertrophy	Pericyte loss BM thickening Microaneurysms New vessel formation

Diabetic Retinopathy

- See also Diabetes Mellitus, page 94
- 1/3 diabetes with > 30 years disease will lose some sight. Diabetics 25 times more likely to go blind
- Risk related to duration ⇒ Type 1 (juvenile onset) more likely to cause damage
- Retinal exam essential:
 - At diagnosis for maturity onset (may have had diabetes for 5 – 10 years)
 - After 5 years for juvenile onset and annually thereafter
 - Fluorescein angiography (injected in arm then photograph retina) to test for neovascularisation
- Causes: Thickened basement membrane of retinal microcirculation → leakage, oedema, nonperfusion and micro-aneurysms
- Macular retinopathy: boggy, leaky macula → blurred vision
- **Non-proliferative retinopathy (= Background Retinopathy):** Progression: oedema (→ blurred vision) → microaneurysms → hard exudates → cotton wool spots → small haemorrhages → venous bleeding
- **Proliferative retinopathy:**
 - Neovascularisation
 - Retinal detachment due to shrinkage of subsequent scars
 - Vitreous haemorrhage (can also be due to vitreous collapse tearing at retina or retinal venous occlusion – usually due to ↑BP → expanded artery → compresses adjacent vein)
- Treatment:
 - Regular checks
 - Blood sugar control
 - Treatment of vascular disease (eg ↓BP)
 - Laser treatment (photocoagulation): 2 – 3,000 burns (but NEVER on macula). ↓O₂ demand → ↓neovascularisation. Complications: ↓peripheral and night vision, macula oedema
 - Vitrectomy: if non-resolving vitreous haemorrhage or fibrovascular contraction of vitreous (which has risk of → retraction of retina → tear)
 - Retinal repair: reattach retina
- Diabetes can also cause: neovascular glaucoma (blocking flow past lens), more susceptible to damage from ↑IOP, cataract, extraocular muscle palsy

Hypertensive Retinopathy

- Rarely causes visual loss. Requires diastolic BP > 120 for many years
- Stages:
 - Stage 0: no changes
 - Stage 1: ‘copper-wiring’ of arterioles due to thickening of the walls due to medial thickening (very subjective)
 - Stage 2: Arteriovenous nipping – thickened arterioles compressing underlying veins
 - Stage 3: Soft-exudates and/or flame haemorrhages (spread longitudinally along fibres)
 - Stage 4: Papilloedema plus the above
- Bilateral and symmetric. More cotton wool spots (nerve fibre hypoxia)
- Retinopathy regresses if hypertension controlled (cf diabetes which doesn’t)
- See also Hypertension, page 34

Tumours

- Can occur on the iris, ciliary body, choroids

Malignant Melanoma of the Choroid

- Presentation: elderly, usually white, visual loss from retinal detachment or incidental
- Retinal appearance: light to darkly pigmented ovoid, elevated mass. Many variants
- 2nd most common site of melanoma after the skin
- Prognosis depends on cell type (Spindle A, Spindle B, Epithelioid or Mixed) and Stage. Overall 50% at 15 years

Retinoblastoma

- Life threatening
- 1:20,000 live births. First few years of life
- Types:
 - 60% sporadic
 - 40% familial (90% bilateral and/or multifocal)
- Presentation: strabismus (squint), ‘white’ patches on papillary/red reflex (leukocoria), red eye
- Pathogenesis:
 - Due to variety of mutations in the tumour suppressor gene RB1 at 13q14 – inactivated a protein which down regulates cell growth
 - Need both alleles to be mutated to cause cancer. Hereditary neuroblastoma = inherit one defective gene from parent, with other allele in one cell undergoing spontaneous mutation. If non-hereditary, need to acquire mutations to both alleles in one cell
- Gross appearance: flat, elevated, diffuse, multicentric pale tumour nodules of plaques
- Microscopic appearance: small round cells with hyperchromatic nuclei, rosettes are characteristic, areas of necrosis and calcification
- Treatment: remove eye
- Complications:
 - Metastasis eg in CNS. From occurrence in eye to spreading down the optic track is ~ 6 months
 - Survivors have a 20% chance of developing malignant tumours at 10 years: osteosarcoma or rhabdomyosarcoma
- Prognosis: 90% 5-year survival (less if optic nerve invasion).

Paediatric Ophthalmology

Assessment

- Vision: fixation (test independently and together), pictures, symbol matching, E
- Alignment: inspection, alternating cover test
- Squint inspection:
 - Corneal reflection when looking at bright light source. Should be in the centre of the pupil on both sides. Cover good eye and see if corneal reflection shifts over the pupil of the bad eye
 - Check for equal sclera on either side of iris. Wide bridge of nose may give pseudo squint
 - Can have squint without amblyopia as long as brain alternates which eye it looks through. If preference for one eye, then amblyopia

Amblyopia

- = “Lazy eye”
- Affects 2 to 3 per 100 children. Can only occur in childhood while visual pathway still developing
- Usually unilateral: maybe bilateral if bad astigmatism or hypermetropia. If unilateral no effect on reading/writing. Treat as insurance against problems in good eye
- Affects central vision: peripheral vision OK
- Three major causes:
 - Squint: Most common cause: misaligned or crossed eyes. The crossed eye is ‘turned off’ to avoid double vision
 - Unequal focus (refractive error). One eye is more near/far sighted or astigmatic
 - Visual obstruction: eg Cataract
 - Also caused by ocular motor defects
- Treatment: force the use of the weak eye by covering the good one (for weeks or months), plus correcting refractive errors with glasses

Refractive errors

- Myopia

- Hypermetropia: if equal and severe then squint due to accommodation
- Stigmatism
- Anisometropia: difference between two eyes (especially if one normal and other long sighted) – accommodation just makes normal eye go out of focus

Other

- Congenital cataract
 - Can be autosomal dominant
 - Check for red reflex within 6 weeks
 - May be uni or bilateral, part of a syndrome or isolated
- Congenital epiphora
 - Watery eye. Common – lacrimal system not fully developed
 - Spontaneous resolution the norm. Conservative treatment until 12 months. Massage +/- antibiotics (stagnation of tear drainage)
- Perinatal eye infections
- Retinoblastoma: See Retinoblastoma, page 147
- Retinopathy of prematurity
 - Very premature babies (low risk if over 30 weeks or 1200 g)
 - Spectrum from severe to norm
 - Problem with vascularisation → retinal detachment over time
- Congenital Glaucoma: rare. One cause of red watery eye

Vestibular

Examination of Eye Movements

- Nystagmus:
 - Peripheral cause: fine, unidirectional, horizontal or rotatory
 - Beats to the side opposite the lesion, worse when looking to that side
 - Named for the direction of the fast phase
 - Is inhibited by fixation (ie will be quicker if you close one eye and try fundoscopy on the other)
 - Bi-directional or vertical nystagmus is always central in origin
- Control of eye movement:
 - Saccades: voluntary quick refixation eye movement. If hypometric then undershot → number of small saccades to catch up. Hypermetric saccades → overshoot → reverse saccade
 - Parietal lobe controls ipsilateral smooth pursuit and contralateral saccades. Impairment over 70 may be normal
 - Impaired pursuit also due to cerebellar and brainstem lesions
- Vestibulo-ocular reflexes:
 - Eye movements to compensate for head movement: maintain stable picture on retina
 - Doll's eye: eyes stay focused on target when head moves

Benign Paroxysmal Positional Vertigo (BPPV)

- Usually posterior semicircular canal. Due to debris in canal (CaCO₃ crystals). Usually cause unknown or aging, but may follow trauma or infection. Fluid movement → distorted stimulations to nerve due to particles → different input from 2 vestibular end organs
- Posterior canals are in the snow-plough position, and are the lowest. Collect debris from the anterior and horizontal canal
- Leads to ↑ discharge to ipsilateral superior oblique and contralateral inferior rectus → torsional nystagmus
- Can also be due to horizontal semicircular canal
- Symptoms:
 - Brief attacks of vertigo precipitated by certain head movements (eg getting into or out of bed, rolling over). Less severe when repeated
 - May spontaneously remit and relapse
 - Hallpike manoeuvre: Rotatory or torsional nystagmus beating toward affected ear when tipped down, after a brief latent period (5 – 10 secs). If immediate then ?central cause. Last about 20 secs and reoccurs again when sitting up. Effect fatigues with retesting (material disperses in process of testing)

- Usually resolves over weeks or months
- No cochlear symptoms
- Treatment:
 - Drug therapy not helpful
 - Canalith Repositioning: induce symptoms → shifts particles into a chamber not sensitive to movement
 - For right ear: sit on edge of bed, turn head 45 degrees to the left, lean all the way down to the right then quickly through 180 degrees to the left, then back to upright. May be easier with eyes closed. Repeat after 2 – 3 minutes. Do every three hours

Acute Peripheral Vestibulopathy

- = Acute labyrinthitis
- Symptoms: acute and continuous vertigo, worse with any movement, lasting several days with nausea and vomiting, but no auditory or neurological symptoms
- Signs: unsteady walking (eg heel-toe). Fine horizontal/rotatory nystagmus beating away from the lesion. Vestibulo-ocular reflex is absent/impaired on passive head rotation toward the lesion, requiring voluntary eye movement to regain fixation (catch-up saccade)
- Most likely to be horizontal canal affected

Other

- Vertigo may follow Head injury. Eg temporal bone fracture tearing 8th nerve
- Infarct with occlusion of the internal auditory artery → affects hearing and balance
- Chronic bilateral vestibulopathy → imbalance and oscillopsia (sensation of the world moving on head movement) due to inadequate vestibulo-ocular reflex. Usually due to gentamycin toxicity
- Migraine may have vestibular symptoms
- MS: vertigo is a classic feature

Ear

External Ear

- Congenital Abnormalities: usually unilateral. Common ones:
 - Preauricular tag: only cosmetic
 - Preauricular sinus: get infected
- Otitis Externa:
 - Localised: furuncle or furunculosis
 - Very painful, may abscess and discharge
 - Usually staph aureus
 - Tx: Oral antibiotics, may need drainage
 - Diffuse (more common)
 - Skin infection: viral or bacterial, or underlying dermatitis (more chronic, less pain and swelling but itchy). If longstanding and treatment resistant, ?fungal (eg aspergillus) – less painful, but blocked and debris, look for hyphae
 - Treatment: swab, clean out canal, topical antibiotics (drops with steroids → ↓swelling)
- Canal trauma from itching, ear cleaning. Resolves spontaneously (unless infected)
- Wax: produced by sebaceous glands (only in the ear) over cartilaginous part. Slightly acid ⇒ antibacterial. Carries debris out
- Insect in ear. Drown it and take out at leisure
- Exostosis: common benign finding. Overgrowth of bone in internal 1/3 of canal, following exposure to cold water (surfers, divers). May → obstruction
- Neoplasms: on pinna: BCC or SCC – require excision

Middle Ear

- Middle ear cleft = ear drum + tympanum + eustachian tube
- Ear drum:
 - Should see malleous, top towards the back
 - May see incus through the drum. If internal jugular very high, may see it at bottom
 - Main part called pars tensa, pars flaccida at top

Otitis Media

- See Acute Otitis Media, page 605

Other Middle Ear Conditions

- Cholesteatoma:
 - Most commonly affects the attic (=epitympanum) and antrum of the mastoid
 - Pars flaccida gets sucked in, expands, erodes surrounding tissue
 - May present with:
 - Chronically discharging, smelly ear, resistant to treatment
 - Conductive hearing loss: ossicles eroded
 - Complication: brain or mastoid abscess
 - Treatment: remove diseased bone
- Otosclerosis:
 - New bone formation fixes the footplate of stapes
 - Conductive hearing loss but ear looks normal
 - F > M, familial, ↑ in pregnancy, menopause
 - 1:20 – 25,000K, can be bilateral
 - Treatment: Stapedectomy (put in piston) or hearing aid
- Tympanic sclerosis. White plaques on ear drum. No consequence
- Barotrauma: from flying/diving. Bleeding and bruising around malleolus. Will settle spontaneously
- Haemotympanum: Blood in middle ear. ?Temporal bone fracture. Battle's Sign (of temporal fracture): bruising behind the pinna

Ear Testing

- Voice Testing
- Tuning fork tests:
 - Rinne Test: 512 Hz fork beside the ear. If conductive loss then bone conduction is better than air conduction. If sensorineural, air conduction best
 - Weber Test: Tuning fork on top of the head. Louder in affected ear if conductive loss, softer in affected ear if sensory loss
- Pure Tone Audiometry:
 - Can establish severity of hearing impairment and whether sensorineural or conductive
 - Measures thresholds across a range of frequencies. Threshold = lowest intensity that can be detected
 - Usually only test in range of conversational speech (250 Hz to 8 KHz)
 - Normal hearing is 0 – 20 dB (zero is based on population surveys)
 - Harder if child aged 3 – 5: need to play games etc
- Auditory Brainstem Response (ABR):
 - Detects evoked potentials in the brainstem in response to sound
 - Used for neonatal testing (reliable from full term), in older kids where behavioural responses are unclear and for testing the auditory nerve (eg acoustic neuroma – but MRI is gold standard, CT with contrast poorer)
- Tympanometry:
 - Measures compliance of middle ear
 - Normal is -100 to 100 daPa
 - Type A: normal (peak compliance over 0 daPa). If peak is low ?scarring or adhesions
 - Type B: Flat curve (ie not compliant at any pressure).
 - Low volume type B: wax impaction or middle ear infusion
 - High volume type B: perforation or grommet
 - Type C: Peak shifted to the left. Eustachian tube obstruction
- Otoacoustic emissions:
 - Test for cochlear function, eg in neonatal screening
 - Also for tinnitus: is it cochlear or non-cochlear
- Paediatric testing:
 - 0 – 3 months: referred from neonatal high-risk register. Need to correct (eg hearing aid implants) by 9 – 10 months otherwise speech impairment
 - 6 – 12 months: distraction testing – looking for head turning, etc
 - 1 – 2½ years: in a room with speakers

Hearing Loss

- See Hearing, page 580 for developmental delay resulting from hearing loss

Congenital Sensorineural Deafness

- Irreversible
- Pathology: problems with nerve or cochlear
- Profound hearing loss at birth: 2 per 1,000
- Most often detected by parents (ie believe them!)
- Aetiology: genetic or acquired, etc:
 - Idiopathic 60%
 - Genetic: most are spontaneous mutations rather than family history
 - Low birth weight
 - Infection (fairly rare now), eg Rubella, also toxoplasmosis, CMV, syphilis
 - Maternal drugs: eg aminoglycosides, alcohol
 - Lots of others, eg hypoxia, high bilirubin

Sudden Onset Sensorineural Hearing Loss

- =Uni/bilateral sudden onset within 3 days. May also get dizzy, tinnitus
- Could be inflammatory, infective, ototoxicity, acoustic neuroma (\Rightarrow always investigate)
- Urgent specialist referral within 24 hours
- Spontaneous remission likely, poor prognosis if elderly, diabetic, vascular disease (Cochlear artery is an end artery – if blocked no collateral flow)

Presbycusis

- = Age related hearing loss, especially at higher frequencies
- Bilateral, symmetrical. May get recruitment (some sounds sound louder – eg toilet flushing, doing dishes)
- M > F, 24% of 64 – 74 year olds, 40% of over 75s
- May have ↓word discrimination: hard to help, ↑volume doesn't help
- Aetiology: age, noise, hypertension, genetic predisposition
- Pathology: degenerative changes, eg of cochlea and also of central procession (this part won't respond to ↑volume)
- Clinical: progressive deafness, 'social' deafness, especially 1 KHz, tinnitus. Often judged worse by spouse/partner
- Exclude: wax impaction, otosclerosis, Paget's disease of the middle ear bones, acoustic neuroma
- Management:
 - Screen elderly people (eg questionnaires or audiology)
 - Hearing aid: only ¼ who would benefit use one, although there are many barriers to use (including cost)
 - Speaking facing the person, clearly, slowly, not too loud, paraphrasing sentences that aren't heard rather than repeating them (also give this advice to spouse and caregivers),
 - Aids (telephone boosters, lights that flash when the doorbell rings, etc)
 - Rehabilitative services available through the Hearing Association

Noise Induced Hearing Loss

- Commonest cause of hearing loss < 60
- Usually industrial noise exposure: factories, builders, firearms, jack hammers
- Safe limit: 80 db for not more than 4 hours
- Classic damage at 4 & 6 KHz on audiogram. Usually bilateral
- Treatment: Prevention, hearing aids not much help

Meniere's Disease

- Diagnostic triad: tinnitus (usually low pitched), deafness, vertigo, (+ feeling of aural fullness)
- Clinical: acute onset of triad, disabling vertigo (world spinning, vomiting) for 6 – 12 hours then low frequency hearing loss
- 30 – 55 years, M > F
- Stages:
 - Early: occasional attacks
 - Later: fluctuating low tone deafness

- End stage: low tone deafness, imbalance but no vertigo
- Pathology: endolymphatic hydrops: distension of endolymphatic space
- Aetiology: unknown. ?↑Production of endolymph
- Diagnosis: possibly nystagmus, fluctuating SN loss
- Treatment: Supportive, low Na diet (\downarrow endolymph), thiazides, antivertigo, antiemetic and histamine medication

Acoustic Neuroma

- Progressive loss of hearing in one ear with tinnitus.
- Not usually associated with \downarrow vestibular function – slow enough to compensate (ie CNS adjusts so world doesn't seem on a tilt). But, everyone with acute vertigo should have a pure tone audiogram to screen for the (rare) possibility of acoustic neuroma
- MRI is definitive, CT is unreliable and should not be done

Aural Rehabilitation

- When hearing loss cannot be corrected, use hearing aids, listening devices and communication strategies

Gastro-Intestinal

- References: Dr Kenwright's Pathology Notes and Gastro Intestinal Run Handbook

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Abdominal Physiology

- Fluid into GI tract each day:
 - Drink 2L
 - Saliva 1L
 - Bile 1 – 1½L
 - Stomach Secretion 1 – 2 L
 - Pancreas 2L
 - Small Bowel 1L
 - 7 – 9 L per day into top end of small bowel
- Output of H₂O in faeces = 150 – 200ml in faeces. 7.5 L absorbed in small intestine. 1- 3 L absorbed in Colon
- Normal stool is 70 – 80% water: held by fibre or in bacteria. ↑Stool H₂O by 25 ml → diarrhoea. ↓By 25 ml → constipation

Abdominal History

- Abdominal Pain:
 - Frequency and duration
 - Site and radiation: pancreas or peptic ulcer may radiate to the back, diaphragm to shoulder and oesophagus to the neck
 - Pattern: colicky pain is due to peristaltic movements against obstruction in bowel or ureters. Biliary pain usually lasts for hours (ie is not colicky)
 - Aggravating or relieving factors, including food, vomiting, defaecation, flatus, lying still in peritonitis
- Appetite and weight change:
 - Anorexia and weight loss ⇒ ?malignancy
 - ↑Appetite and weight loss ⇒ ?malabsorption
- Nausea and vomiting, ask about vomit (blood, bile, old food ⇒ outlet obstruction, etc)
- Heartburn and acid regurgitation
- Dysphagia: differentiate painful swallowing from actual difficulty
- Diarrhoea: check frequency and consistency. Can be:
 - Secretory diarrhoea: large volume
 - Osmotic diarrhoea: disappears with fasting
 - Abnormal intestinal motility
 - Exudative diarrhoea: with blood or mucus
 - Malabsorption: steatorrhoea
- Constipation: Check what they mean. Check drugs, hypothyroidism, diabetes, etc. Is it recent (cancer can cause obstruction)?
- Mucus: ?IBS or rectal ulcer, fistula or villous adenoma
- Bleeding:
 - Haematemesis (vomiting blood)
 - Melena (jet black stools)
 - Haematochezia (bright red rectal bleeding)
- Jaundice: also ask about dark urine and pale stools (→ obstructive jaundice)
- Pruritis: itching skin. Can be caused by cholestatic liver disease
- Abdominal swelling. Also check ankles
- Lethargy: common in liver disease
- Drugs: especially NSAIDS
- Social history: alcohol, occupational exposure to hepatitis, travel, sexual and recreational drug history

Abdominal Exam

- Trying to filter symptoms for:
 - Upper vs. lower
 - Functional (motility) vs. structural (infection etc)
 - Alarm symptoms

Periphery

- General:
 - Lie flat and comfortable (\rightarrow relaxed muscles)
 - General appearance:
 - Jaundice
 - Weight and wasting (weight them)
 - Skin: pigmentation (eg haemochromatosis)
 - Mental state: hepatic encephalopathy
- Hands for peripheral stigmata of abdominal disease (mainly liver):
 - Nails: Leuconychia (nail bed opacity in hypoalbuminaemia), clubbing in cirrhosis
 - Palms: Palmar erythema (reddened palms) in chronic liver disease, anaemia (from GI loss, malabsorption or chronic disease)
 - Dupuytren's Contracture: thickening of the palmar fascia \rightarrow permanent flexion, especially of the ring finger. In manual workers, alcohol, and familial
 - Hepatic flap: extend wrists and separate fingers for 15 seconds
- Arms:
 - Bruising:
 - Large bruises (ecchymoses) from clotting disorders
 - Small bruises (petechiae) from alcohol toxicity \rightarrow ↓ platelets (also portal hypertension \rightarrow splenomegaly \rightarrow ↓ platelets)
 - Also muscle wasting, scratch marks, spider naevi (cirrhosis – usually alcohol, due to oestrogen excess)
- Face:
 - Eyes for jaundice, anaemia, or scleritis/iritis (associated with inflammatory bowel disease)
 - Bilateral swollen parotids due to fatty infiltration with ↑ alcohol
 - Smell of breath: fetor hepaticus (sweet smell) or alcohol
 - Ulceration (eg in Crohn's) or candida in the mouth
 - Angular stomatitis: cracks at the corners of the mouth: causes include Vit B 6 and 12, folate and iron deficiency
- Neck and Chest:
 - JVP
 - Cervical lymph nodes and especially supraclavicular nodes (always bad)
 - Gynaecomastia: due to ↑ oestrogen to testosterone ratio (alcoholic effect on Leydig cells), or due to spironolactone (used to treat ascites)
- Examine chest:
 - Gynaecomastia
 - Spider naevi
 - Body hair

Abdomen

- Regions:
 - Right & left hypochondrium, epigastrium
 - Right & left lumbar/mid-lateral region
 - Right & left iliac fossa, hypogastrium or suprapubic
- Why examine:
 - Enlarged organs
 - Abnormal masses (e.g. tumour or inflammation – abscess) & fluid (ascites)
 - Signs of peritoneal irritation (hurts with cough)
 - Hernia
- Inspection:
 - ?Abdomen moves with respiration (look from side on to view asymmetry \Rightarrow ?mass)
 - Scars: what were operations
 - Hernias - Hernial Orifices: Umbilical, Inguinal, femoral
 - Visible lumps/organs
 - Skin lesions/pigmentation (eg Shingles causes strange pains until it erupts)
 - Distension: Due to Fat, Fluid, Fetus, Flatus, Faeces, Filthy big tumour. Umbilicus is shallow or everted in ascites or pregnancy

- Veins. Test direction of flow. In portal hypertension, flow is away from umbilicus (rare, = Caput Medusae). In IVC obstruction, flow is upwards
- Striae: Ascites, pregnancy, recent weight loss, rarely Cushing's Syndrome
- Pulsitations: abdominal aorta. Visible in thin people. If fat then ?aneurysm
- Palpation:
 - Relax patient, use warm hands. Bend knees up if necessary to relax muscles
 - Gently all round: look at face – check for tenderness/peritonism, obvious lumps. Do most painful quadrant last. If tense, use their hand
 - Percuss before palpation for organs. Check for shifting dullness
 - More firmly: looking for organs, masses
- What to palpate for:
 - Liver:
 - Don't usually feel in normal adult, may in child. Normal span in mid-clavicular line is 10 - 12 cm. Don't measure on lateral side, right lobe hangs down in some giving appearance of bigger liver (Riedel's lobe)
 - Describe as hard or soft, tender or non-tender, regular or irregular, pulsatile or non-pulsatile
 - Spleen: needs to be enlarged 3 or 4 times to palpate. Palpable spleen is ALWAYS bad. Start palpation inferior to the umbilicus
 - Kidney: if palpable either tumour or obstructed
 - Aorta: can nearly palpate in most people – key issue is width
 - Gallbladder: Murphy's sign: lay fingers along costal margin, patient takes a deep breath and it hurts. Enlarged gallbladder is unlikely to be gallstones as chronic gallstones → fibrosis that can't then expand. Instead, ?carcinoma of the head of the pancreas.
 - Also palpate for bladder, uterus
- What to note: Site, size, shape, consistency, tender, pulsatile
- Signs of inflammation, infection or haemorrhage:
 - Tenderness: how severe is pain in response to pressure
 - Guarding: muscles resist pressure. Can be voluntary or involuntary (latter suggests peritonitis)
 - Rigidity: muscles tight
 - Rebound tenderness: push down surreptitiously then remove hand quickly – watch face for pain (peritonitis)
- Percuss for:
 - Liver
 - Spleen: unreliable
 - Kidneys: but overlying bowel makes this problematic
 - Bladder: supra-pubic dullness indicates upper border of an enlarged bladder or pelvic mass
 - Shifting dullness in ascites
- Auscultate:
 - Bowel sounds: just below umbilicus. Are either present or absent (increased or decreased meaningless)
 - Over liver, spleen, renal areas for rubs and bruits
- Groin: genitalia, lymph nodes, hernial orifices
- Rectal:
 - Observe for tags, haemorrhoids, pylonodal sinuses, blood, faeces colour
 - Feel for anal tone, masses or strictures in the rectum
- Legs: bruising, muscle wasting, oedema (check sacral as well)

Causes of Splenomegaly

- Chronic granulocytic leukaemia
- Malaria
- Lymphoma
- Myelofibrosis
- Polycythaemia

Abdominal Tests

Abdominal X-ray

- Gas:
 - Normal in colon and stomach, some in small bowel OK
 - Define colon: has hastrations – but don't cross tinea coli. Only part of bowel with faeces
 - If they have ulcerative colitis shouldn't be bigger than 5cm – otherwise toxic megacolon
 - Transverse diameter of caecum shouldn't be bigger than 9 cm otherwise risk of rupture
 - Small bowel: circularis goes right round. Max diameter 3 cm. Gas if obstructed, diarrhoea, ileus or swallowing gas due to pain
 - Gas under diaphragm = pneumo-peritoneum
 - Can have gas in biliary tree (esp. after ERCP, or if fistula to bowel), and retroperitoneal from perforated 2nd part of duodenum
- Stripes:
 - Edges of psoas: demarcated against fat
 - Lateral abdominal wall: flank line is peritoneum. If exudate in the paracolic gutter then distance from the colon is increased
 - Renal outline: parallel to upper psoas
 - Edge of liver
 - Edge of spleen (not always seen)
- Stones:
 - Any extraosseous calcifications
 - Bladder, kidney, gallbladder
- Bones

Other Abdominal Tests

Endoscopy

- Complications: Mallory Weiss tear, perforation (1/2000), aspiration pneumonia (rare)

Ultrasound for Ascites

- Need 1 litre of fluid before it can be detected

Rectal biopsy

- For ulcerative colitis, microscopic colitis, amyloidosis, cancer

Stool test

- Occult blood
- Culture (for bacteria): would either be self-limiting or very sick
- Ova, parasites & giardia antigen: if high risk, repeat 3 times. Needs to be warm on arrival in lab

Barium Enema

- Make sure they got to the caecum (i.e. want to see contrast in the appendix or terminal ileum)
- Also need to know that bowel was clean enough for them not to miss anything

Developmental Abnormalities

- See Congenital abnormalities, page 639

Oral Pathology

- Same pathology in the mouth as with skin, mucosa, nerves, blood vessels, etc. But also specialised stuff
- Teeth and Teeth forming tissue:
 - Genetic defects
 - Severe illness eg measles → bands on teeth
 - Tetracycline → discolouration
 - Vomiting, regurgitation (eg bulimia) → erosion
 - Cysts or tumours of teeth forming tissue (eg ameloblastoma)

- Gums: lose more teeth through gum disease than caries. Immunosuppressive disease can lead to abnormal gums (eg leukaemia)
- Salivary glands:
 - Calcification in duct of major gland → blockage
 - Tumours/cysts
 - Recurrent infections: short/wide ducts → retrograde flow → infection with oral commensals
 - Post-radiotherapy to head and neck. Salivary tissue very sensitive → dry mouth
 - Drug induced dry mouth: made worse by anxiety, smoking, dehydration
 - Sjogren's Disease: autoimmune attack of salivary and lacrimal glands
 - Dry mouth → rapid tooth decay (no buffering from saliva)
- Oral Mucosa:
 - Hyperkeratosis with hyperplasia or atrophy: looks white
 - Upsets to normal flora. Eg candida overgrowth. Can lead to loss of papilla (atrophic candidiasis), hyperkeratosis
 - Ulceration: lots of causes: eg trauma (new dentures, burns), herpes, Aphthous ulcers (if recurrent then check ↓ serum ferritin, hormonal cycle, stress, food allergy [eg benzoic acid in Coca Cola], heredity)
 - White lesions (due to thickened keratin layer):
 - Lichen Planus: white patches surround by red erosions
 - Lichenoid drug reactions
 - Malignant and premalignant (eg leukoplakia - white, erythroplakia – red). Eg squamous cell carcinoma. Related to smoking – 60 – 75% of white lesions go away if they stop

Oesophagus

Dysphagia

- =Difficulty swallowing
- Define level and whether progressive or intermittent
- History: Time course, reflux symptoms, cough, asthma, chest infections, weight loss, pain
- Examination:
 - Lymphadenopathy
 - Chest signs: consolidation, effusion
 - Hepatomegaly
 - Ascites
 - Raynaud's: connective tissue disorders
- Investigations:
 - Barium swallow (video)
 - CT scan: staging malignancy
 - Endoscopy: assess mucosa, strictures
 - Manometry: assess motility
- Oesophageal motility causes:
 - Fluids get through OK, solids the problem
 - Pharynx: neurological diseases causing failure of high pressure contraction
 - Cricopharyngeal sphincter: failure due to cricopharyngeal spasm or pharyngeal pouch
 - Oesophagus: failure of peristaltic wave due to diffuse oesophageal spasm
 - Cardiac sphincter: failure of opening due to achalasia
- Oesophageal obstruction causes:
 - Fluids also a problem
 - Extrinsic compression: thyroid, other neck mass, lymph nodes (Ca lung)
 - Carcinoma of the oesophagus. Often diagnosed at advanced stage. Either squamous or adenocarcinoma. Diagnosis by endoscopy + biopsy +/- CT. Treatment – surgical reconstruction. Palliation: radiation + internal stent
 - Reflux stricture of the lower oesophagus

Oesophageal Tumours

- Symptoms & signs:
 - Dysphagia: when disease advanced
 - Inability to swallow saliva

- Pain
- Weight loss, anaemia, lymphadenopathy, hepatomegaly
- Investigations:
 - Endoscopy: biopsy
 - Bloods: FBC (anaemia), ALP (metastases in liver or bone)
 - CT, MRI: localised tumours
- Differential diagnosis:
 - Benign stricture
 - Motility disorders, especially achalasia
 - Extrinsic compression of oesophagus (e.g. bronchial carcinoma)
- Treatment:
 - Adequate nutrition (enteral feeding tube if necessary)
 - Pain management
 - Surgery/radiotherapy: usually only palliative
- Squamous cell carcinoma:
 - 90 % of oesophageal cancer
 - Epidemiology: M>F 4:1, B>W, approx 5 per 100,000
 - Aetiology: dietary (fungal, nitrates, ↓ leafy greens), oesophagitis, alcohol, tobacco, genetics
 - Macroscopic appearance: Site: 50% middle, 30% lower, 20% upper. Early lesion a small grey-white thickening. Later: fungating tumour, ulceration, infiltration (may present as stricture)
 - Microscopic appearance:
 - Sheets of neoplastic squamous cells with intercellular bridges
 - Keratin whorls ⇒ well differentiated
 - Mitoses, necrosis, pleomorphism (as with all malignant tumours)
 - Invasion of mediastinal structures and lymphatics
 - Clinical outcome: Insidious (→ late presentation). 70% dead at one year
- Adenocarcinoma of the oesophagus:
 - 10% of oesophageal carcinomas. Arise in Barrett's mucosa
 - Elderly, mainly males
 - Macroscopic: mass or nodule
 - Microscopic: pleomorphism, irregular gland formation

Achalasia

- = Failure to relax lower sphincter
- Symptoms & signs
 - Dysphagia: with both solids and liquids
 - Intermittent chest pain
 - Regurgitation/reflux
 - Weight loss
 - Nocturnal cough (related to regurgitation & aspiration)
- Investigations
 - Chest x-ray: dilated oesophagus
 - Barium swallow: delayed passage through cardia, oesophageal dilation
 - Endoscopy: may be normal, may be food in oesophagus (→ secondary oesophagitis)
 - Manometry: impaired relaxation of lower oesophageal sphincter, absent peristalsis
- Differential diagnosis
 - Benign or malignant stricture
 - Malignancy at cardia
- Treatment
 - Medical: nitrates and calcium antagonists → ↓ sphincter pressure
 - Balloon Dilation
 - Botulinus toxin injection
 - Cardiomotomy
 - Retrosternal pain may continue following treatment. May need H2 antagonist

Dyspepsia

- = Upper abdominal discomfort. Includes bloating, fullness, early satiety, nausea, anorexia, heartburn, regurgitation. Chronic not acute.

- Exclude biliary colic, pancreas and heart pain
- Functional/idiopathic/essential dyspepsia = all investigations normal but still pain = Up to 60% of dyspepsia. ?Increased visceral sensitivity, ?delayed gastric emptying, ?H Pylori gastritis
- Abdominal pain without significant pathology very common
- Ask about weight: if overweight – think reflux, if loosing weight think cancer
- Oesophagitis doesn't cause anaemia until proved otherwise
- Types:
 - Reflux like → heartburn/regurgitation – treat with empiric H2 antagonist
 - Dysmotility like → bloating, nausea, fullness (?delayed gastric emptying) – treat with prokinetics (e.g. cisapride & domperidone)

Oesophagitis

- Caused by:
 - Reflux oesophagitis
 - Irritants (eg alcohol, tobacco)
 - Fungal or viral infection
 - Systemic blistering diseases (rare)
 - Radiation (eg for breast cancer) or cytotoxics
 - Graft vs. host disease (affects whole GI)

Gastro-Oesophageal Reflux Disease (GORD)

- Includes reflux oesophagitis
- An acid and motility disease
- Mechanisms for reflux:
 - Lowered sphincter pressure/incompetence: Aggravated by large meals, acidic (e.g. citrus), fatty food, chocolate, smoking, peppermint, caffeine
 - ↑Abdominal pressure: effects right crus of diaphragm which acts like an external LOS: aggravated by obesity, straining, pregnancy, bending over
- Presentation:
 - Heart burn
 - Dyspepsia, nocturnal cough or chest pain
 - Poor correlation between symptoms and severity
- Diagnosis:
 - Therapeutic trial
 - If going to investigate, don't treat in meantime: otherwise → ↓inflammation (if any)
 - Endoscopy most sensitive and specific: use after failure of therapeutic trial or if alarm symptoms. Biopsy only to exclude malignancy or Barrett's oesophagus. 50% are normal on endoscopy
 - Gold standard: 24 hour ambulatory pH monitoring
 - Lesions graded 1 (mild) to 4 (severe), 5 (metaplasia – Barrett's). If Grade ≥ 3 , then indefinite, significant acid suppression.
- Alarm Symptoms:
 - Dysphagia
 - Early satiety
 - Night waking
 - Abrupt onset
 - Recurrent hoarseness
 - ↑Severity
 - Weight loss
 - Vomiting blood
 - Symptoms for the first time > 45 years or soon after any treatment
- Differential: Peptic ulcer, gastric or oesophageal cancer, angina/IHD, hiatus hernia
- Macroscopic appearance: Oedema, hyperaemia (redness), ulceration, white patches with candida
- Microscopic appearance:
 - Intraepithelial eosinophils
 - Neutrophils in the epithelium and lamina propria
 - Regenerative and degenerative features of the epithelium (\rightarrow thickening)
 - Ulceration

- Treatment hierarchy:
 - Try antacids & lifestyle changes first (e.g. tilt bed, no food before bed, avoid problem foods, weight loss)
 - Paracetamol for pain not aspirin
 - High fibre diet: reduces straining → reduces reflux due to ↓ intra-abdominal pressure (only helps if straining to start with)
 - Prokinetics: cisapride, metoclopramide or domperidone
 - H2 antagonists (OK for mild): healing after 8 – 12 weeks
 - PPI (more effective in severe): omeprazole, lansoprazole, pantoprazole
 - Nissen fundoplication (operation): also reduces hiatus hernia at same time
- Complications:
 - Barrett's oesophagus: long-standing reflux → Metaplasia: columnar changes above gastro-oesophageal junction. Predisposes to cancer
 - Ulceration, stricture (always biopsy strictures as some cancers present like this)
 - Adenocarcinoma

Hiatus Hernia

- Common. May be asymptomatic
- Two types: sliding or rolling/para-oesophageal
- Symptoms:
 - Sliding: Reflux, cardiac and pulmonary symptoms (mass in thoracic cavity)
 - Rolling: cardiac and pulmonary symptoms, dysphagia, hiccup, volvulus

Stomach and Duodenum

Gastritis

- Acute gastritis:
 - Transient, acute, mucosal inflammation
 - Causes: aspirin, alcohol, chemotherapy, stress, shock, severe systemic infection
 - Macroscopic appearance: oedema, hyperaemia, superficial erosion
 - Microscopic appearance: neutrophils, sloughing, haemorrhage in the lamina propria
- Chronic gastritis:
 - Lost velvety appearance, flat (no folds)
 - Autoimmune type: Associated with antibodies to parietal cells (→ achlorhydria) and intrinsic factor. Pernicious anaemia develops in 10%. Usually affects body of the stomach
 - Helicobacter pylori infection:
 - Hypertrophic gastritis: enlargement of rugal folds due to hyperplasia. Several causes. Differential: lymphoma can also present with enlargement of rugae

Acute Ulcers

- Stress ulcers: shock, burns, sepsis
- Due to mucosal hypoxia
- Usually heal quickly
- Appearance: multiple circular ulcers < 1cm. Penetrate submucosa. Occasionally massive bleeding

Peptic (Gastric & Duodenal) Ulcer

Symptoms & Signs

- Gastric & duodenal usually indistinguishable clinically
- Uncomplicated: can be silent, epigastric pain after food, relieved by antacids, and waking at night due to pain, weight change
- Complicated: haematemesis/melaena, vomiting, severe pain ⇒ pancreatitis or perforation (but 50% of patients with fatal complications present without ulcer pain), shock, anaemia, peritonitis

Epidemiology

- 10% of the population have one at some time in their lives
- M>F 3:1
- Genetic risk (50% twin concordance)

Aetiology

- Need mucosal injury
- H. Pylori infection. Damages D cells → ↑gastrin → ↑acid & pepsin → metaplasia + helicobacter damage → ulcer
- Smoking, alcohol, etc
- NSAIDs
- If neither H. Pylori infection nor NSAIDs then ulcer very unlikely
- Not due to ↑acid (except for Zollinger-Ellison syndrome)
- Macroscopic appearance: well demarcated, punched out, with radiating mucosal folds. Most <4 cm diameter
- Microscopic appearance – 4 layers/zones:
 - Exudative zone: fibrin, debris, neutrophils, etc
 - Necrotic zone: necrotic debris
 - Granulation tissue zone
 - Zone of fibrous tissue
 - Adjacent: blood vessel thickening, mucosal hyperplasia, chronic inflammation

Helicobacter Pylori

- Curved gram negative organisms in gastric mucus
- From contaminated water
- Prevalence in NZ 30% but declining, 20% in Wellington, lower in Dunedin. Causes 60% of antral gastritis (other causes include bile reflux)
- H. Pylori infection in 70-80% of gastric ulcers, 95% of duodenal
- Also associated with gastric adenocarcinoma and gastric MALT lymphoma (i.e. it's a carcinogen)
- Lives beneath gastric mucus: pH of 5 – 7 (compared with 1 – 2 in stomach lumen)
- H. Pylori always gives gastritis, usually in the antrum, but usually asymptomatic. Eradication only of benefit if ulcer's present
- Microscopic appearance: chronic atrophic gastritis. Chronic inflammatory infiltrate → gland atrophy over time, intestinal metaplasia of remaining glands

Investigations

- Bloods: FBC (anaemia), amylase
- Refer for endoscopy if > 45 years or alarm symptoms (See Gastro-Oesophageal Reflux Disease (GORD), page 160)
- At endoscopy check for H Pylori, CLO test from biopsy sample, or histology/culture, and biopsy from antrum of stomach. 1% of gastric ulcers are cancers – always biopsy – but ulcers don't predispose to cancer
- Urease breath test (gold standard): swallow C13 labelled urease and check for expired labelled CO₂. H. Pylori has Urease to turn urea → NH₂ + CO₂
- CXR: subdiaphragmatic gas in perforation
- Contrast Xray (less accurate than endoscopy)

Differential

- Pain: Reflux, gastric ulcer, gastric cancer, gallbladder disease, chronic pancreatitis, IBS
- Acute Severe Pain: acute pancreatitis, biliary colic, aortic dissection, MI
- Zollinger-Ellison syndrome: uncontrolled gastric acid secretion driven by ↑plasma gastrin released by a gastrinoma - 50% malignant → multiple peptic ulcers
- Crohn's, Lymphoma, CMV

Treatment

- If on NSAIDs: stop them. Normally curative
- Antacids
- H₂ receptor antagonists: good healing over 4 – 8 weeks (ranitidine, cimetidine)
- PPIs: for unresponsive ulcers - superior to H₂RA for healing and maintenance
- Triple therapy for H. Pylori:
 - 75% effective under normal conditions. Reinfection is rare (< 1%)
 - 2 weeks optimal – 7 days pretty good
 - pH has effect on antibiotic bioavailability: want to ↑pH (e.g. omeprazole)
 - Bismuth (De-Nol) + tetracycline & metronidazole + ranitidine, or

- Clarithromycin & metronidazole + ranitidine, or
- Amoxycillin + metronidazole + omeprazole
- Treatment of H. Pylori in non-ulcer dyspepsia has little effect. Only proven benefit of eradication is in ulcer disease and MALT lymphoma
- Always re-scope an ulcer to check healing. You want to be sure it's not a cancer missed on histology (and PPIs will mask symptoms)

Complications

- Only time surgery is involved
- Haemorrhage: 2.5% of PU per year → occult, melaena or haematemesis. 10% mortality
- Perforation: 1% of PU per year, usually NSAID users
- Penetrating: pancreas, liver, biliary
- Obstruction: of pylorus due to chronic scarring/stenosis → functional obstruction

Pernicious Anaemia

- Symptoms & signs (due to anaemia or B12 deficiency):
 - SOB/lethargy
 - Sore tongue (glossitis in 50%)
 - Parasthesiae and gait disturbance (peripheral neuropathy), loss of proprioception/reflexes
 - Depression, impaired memory
 - Mild splenomegaly
- Investigations:
 - Bloods: macrocytic anaemia, leucopenia, hypersegmented neutrophils, ↑bilirubin, ↓serum B12
 - Schilling Test: < 10% urinary excretion of ⁵⁸Co labelled B12, corrected when administered with intrinsic factor
 - Also serum gastrin measurement and endoscopy for gastritis
- Differential:
 - Dietary (e.g. vegan) or malabsorption (e.g. Crohn's) deficiency of B12
 - Chronic H Pylori gastritis
 - 8% of pernicious anaemias develop gastric cancer
- Treatment: iv B12, loading dose then 1 mg every 3 months (watch for folate deficiency initially)

Gastric Neoplasia

- Symptoms & Signs
 - 'Ulcer-like dyspepsia' lasting more than a few weeks in middle aged or older
 - Early satiety, fullness ⇒ small cancer in pylorus, large in body of stomach, extrinsic compression, or limitis plastica (infiltrates stomach so can't distend)
 - Vomiting, haematemesis/melaena
 - Weight loss, malaise
 - Anaemia
 - Metastases: Knobbly enlarged liver, ascites, pleural effusion, left anterior axillary node
- Investigations:
 - FBC (anaemia), LFT (mets?)
 - Endoscopy: biopsy and assess obstruction
 - CT/ultrasound to assess metastases
- Differential:
 - Ulcer or non-ulcer dyspepsia
 - Reflux oesophagitis
 - Anaemia of other causes
 - Depression
- Types:
 - Benign Tumours:
 - Polyps: hyperplastic/inflammatory – 90%, Neoplastic/adenomatous – 10%
 - Stromal tumours: leiomyomas, etc
 - Gastric Carcinoma:
 - Epidemiology: high in Japan (due to diet → screening programme), China, decreasing in Western world (better water → ↓helicobacter and better food preservation → ↓oxidised food which is carcinogenic). 6/100,000. M > F

- Aetiology: Diet (\uparrow pickles, \uparrow smoked food, \downarrow green leafy vegetables), genetic, associated with chronic gastritis and adenomatous polyps, and helicobacter
- Evolution: dysplasia \rightarrow carcinoma-in-situ (confined to submucosa) \rightarrow invasive
- Macroscopic: Early – thickening, hyperaemia. Go on to 1) ulcerating, fungating masses, rolled overhanging edge, 2) diffusely infiltrative (limitis plastica – “leather bottle stomach” – thickened wall and folds), 3) polypoid mass
- Microscopic appearance: 1) Intestinal type: malignant glands, 2) Diffuse or gastric type: cygnet ring cells
- Outcome: depends on stage not type. Metastasis to lymph nodes, peritoneum, liver, lungs
- Treatment:
 - Resection
 - Chemotherapy for palliation only
 - Symptomatic drug treatment

Celiac Disease

- = Gluten sensitive enteropathy: sensitive to gliaden protein fraction in gluten (found in BROW: barley, rye, oats and wheat)

Epidemiology

- In Wgtn: prevalence 70 per 100,000, incidence 1.8 per 100,000
- Male:female = 1:3
- 10% familial recurrence
- Association with HLA 8

Symptoms

- Abdominal pain (related to meals), diarrhoea, steatorrhoea, no fever, sudden onset, early satiety, vomiting
- Symptoms secondary to malabsorption: anaemia (common presentation – Fe absorbed in duodenum), failure to thrive, weight loss, tetany, osteoporosis (\downarrow Ca or Mg), Wernicke's encephalopathy
- Clubbing

Diagnosis

- Bloods: ferritin, folate, B12, and Ca
- Faecal fat
- Contrast Xray
- Antigliadin IgG antibodies
- Antigliadin IgA antibodies
- Endomysial antibodies: high predictive value
- Diagnosis: histology + histological improvement on gluten-free diet

Differential

- Other causes of diarrhoea: e.g. Lactose intolerance, IBD, IBS
- Thyrotoxicosis (\rightarrow \uparrow bowel motility)
- \uparrow Ca

Aetiology

- Dietary factors + environmental agents + genetic pre-disposition (HLA B8, DR3, Celtic ancestry) \rightarrow Latent-compensated gluten sensitivity (proximal only, B12 absorbed in terminal ileum) \rightarrow Unmasking factors (nutrient deficiency, metabolic stress, infections, etc) \rightarrow Symptomatic

Pathology

- Subtotal villous atrophy
- Crypt hyperplasia
- Leading to abnormal small bowel mucosa and malabsorption. Primarily affects distal duodenum. In severe cases can extend to terminal ileum

Treatment

- Gluten free diet for life: refer to dietician
- If severe, prednisone

- Replenish deficiencies: iron, folate, vitamins
- Bones: due to Ca malabsorption – do bone scan, Ca supplements. A diary free diet pre-diagnosis may have improved things as less lactase in coeliac disease
- ?Family screening: but antibodies only +ive with mucosal damage (doesn't detect latent disease). Keep kids growth charts up to date
- Refer patients to Celiac Society

Other Malabsorption Syndromes

- Lactose Intolerance:
 - Lactose intolerance very common: especially where dairy products are uncommon. Either congenital (rare), acquired, or secondary to enteritis (i.e. be careful with milk for several weeks after bad diarrhoea)
 - Lactose breath test: Give lactose. Broken down by lactase. If ↓lactase then osmotic diarrhoea → rapid transit → early & large rise in H₂ as lactose is broken down by bacteria. Check with serial breath H₂ measurements
- Tropical Sprue: Enterotoxic E coli infection in visitors to the tropics. Affects distal intestine
- Whipple's Disease: Tropheryma whippelii (bacteria) infection. Obstruction to lymphatics causes malabsorption. Treat with erythromycin, otherwise death from systemic spread
- Abetalipoproteinaemia: genetic defect, unable to synthesise apoproteins

Small & Large Bowel

Pathology

- Differentiating small and large bowel: large bowel has teniae coli, and haustra are not continuous around inside of lumen
- Type of colitis:
 - Infective
 - Collagenous
 - Microscopic
 - Pseudomembranous
 - Acute & chronic irradiation
 - Necrotising enterocolitis
 - Ischaemic
 - Amoebiasis
 - Crohn's and Ulcerative
- Gut layers:
 - Mucosa and muscularis mucosa
 - Submucosa with lamina propria
 - Muscularis propria (two layers)
 - Serosa/adventitia
- Melanosis Colis: brown cells at base of crypts - lipofuscin from broken down organelles, correlated with laxative use, no impact

Ischaemic Bowel Disease

- Distribution:
 - Vascular occlusion: superior mesenteric
 - Watershed lesions (eg splenic flexure, rectum)
- Transmural infarction:
 - Pathogenesis: arterial thrombosis, embolic occlusion, venous thrombosis or strangulation and torsion
 - Macroscopic appearance: Red and intensely congested. Subsequently gangrenous
 - Microscopic appearance: transmural necrosis, congested with blood, epithelium sloughed off, inflammation, perforation in 3 – 4 days
 - Clinical: severe pain, nausea, collapse, 50 – 75% die
- Mucosal Infarction:
 - Pathogenesis: non-occlusive hypoperfusion damaging only the inner layers due to shock, cardiac failure, etc

- Macroscopic appearance: congested in patches or large areas. Mucosa haemorrhagic, oedematous, ulcerated
- Microscopic appearance: Necrosis of mucosa, remainder OK
- Clinical: pain, bloody diarrhoea, shock, potentially reversible

Bowel Obstruction

Presentation

- High small bowel: mainly vomiting, less distension/pain, no constipation, more rapid onset
- Low large bowel: mainly distension/constipation/pain, evolves over days/week ('sub-acute')
- Visceral pain ⇒ poorly localised to either epigastric, peri-umbilical or subrapubic regions

Classification

- Small vs. Large
- Complete vs. Incomplete
- Open loop vs. closed loop
 - Open loop: mainly colicky pain – comes in waves. Either top end or bottom end still open
 - Closed loop:
 - Isolated loop → ↑peristalsis & ↑fluid → ↑intramural pressure → ↓capillary perfusion & compromised venous drainage → gangrene → perforation (rapidly fatal through sepsis and mass cytokine release)
 - Symptoms: quick (6 hours start to finish), constant severe pain that started colicky, ↑temperature & ↑pulse once infarction starts
 - X-rays & WBCs may be normal
 - Differential diagnosis pancreatitis (do amylase)

Causes

- Intraluminal: e.g.
 - Choleocystoduodenal fistula → gallstone ileus. Gallstone moves from gallbladder to duodenum via fistula (→ air into biliary tree). Also following ERCP
 - Bezoar: lump of stuff (e.g. hair) intermittently blocking ileocaecal valve
- In the bowel wall:
 - Crohn's
 - Tb
 - Tumours of small bowel. (Less common) – lymphoma, carcinoid (neuro-endocrine), adenocarcinoma, melanoma secondaries
- Outside wall
 - Hernia of small bowel, especially indirect inguinal or femoral (⇒ always examine groin)
 - Adhesion from previous surgery (⇒ look for scars): can take years to present acutely
 - Small bowel volvulus: malrotation of embryonic mesentery (can also be acquired, e.g. drugs) → easy rotation of mesentery
 - Intussusception: piece of bowel forced into distal section. Rare, most common in kids (2 months → 2 years). Especially around ileocaecal valve
- Also in large bowel:
 - Diverticular stricture and cancer (most common in sigmoid)
 - Volvulus: of any part of colon (especially sigmoid)
 - Distal obstruction can also cause ileocaecal valve to shut → close loop obstruction. Caecum ischaemic first as biggest radius (Law of La Place)
 - Pseudo-obstruction: motility problem (esp. after recent surgery). Check with barium enema, contrast will go through OK but rectum will be empty

Management

- History: bowel movements, previous surgery, weight loss
- Exam: dehydration (from vomiting) & distension
- Treatment:
 - Rehydration: crystalloid (i.e. saline) – only want to restore ECF (i.e. not dextrose)
 - Nasogastric tube: suck out stomach contents → ↓vomiting & aspiration
 - Urinary catheter: monitor fluids
 - Monitor creatinine: if hypoperfusion → kidney failure

- FBC: group & save
- Pain relief: 10 mg im morphine or slow infusion. If dose is bad enough to need another then need surgery
- If no scars & no hernias → surgery
- If scars → may settle (if operate → more adhesions). Regular review

Appendicitis

- = Acute Suppurative Appendicitis
- Lifetime incidence = 6%
- Most common surgical emergency
- Incidence declining (?↑Hygiene → ↓pathogen exposure)
- Gut organisms invade appendix wall after lumen obstruction
- If suspected then nil by mouth. If no diarrhoea or vomiting then no immediate danger of dehydration
- If you diagnose it, or if you don't, you'll be wrong 50% of the time!

Symptoms & Signs

- Very difficult to diagnose – considerable variety in presentation
- Fever: 37.5 – 38.5. Typically low grade. Higher if perforated. Swinging fever more typical of an abscess
- Pain:
 - Initially: central abdominal colic (obstructed appendix and ↑lumen pressure)
 - Ball-valve relief of obstruction often leads to colicky pain
 - Once peritoneum inflamed: constant RIF pain.
 - If perforated: generalised tenderness, maybe distension. If really sick, abdomen may not be hard
 - However, considerable variation – pain may stay central, may be situated elsewhere in abdomen
 - Lying on back and lying still, coughing hurts (peritonitis)
 - Push on left side → hurts more on right
 - Evoking pain: cough or **hop on right leg**. In a child, look for tenderness and guarding – *not* rebound – won't let anyone touch them after that.
- Systemic signs:
 - Kids: vague pain, off food (won't eat favourite food), diarrhoea, vomiting
 - Elderly: shocked, confused, no pain
 - Anorexia, maybe vomiting
 - Constipation or diarrhoea
 - Tachycardia (not always)
- May be urinary symptoms and signs: especially in children with appendix in the pelvis – e.g. dysuria, white cells in urine (always do dipstick)

Differential

- Appendicitis may co-exist with acute tonsillitis, pneumonia, UTI or even gastro-enteritis
- Salpingitis in female, ectopic pregnancy, food poisoning, diverticulitis, cholecystitis, perforated ulcer, cystitis, Crohn's disease, inflammation of Meikels diverticulum (if operate and appendix OK, always check a metre up the small bowel), radiation of torsion of right testis, strangulated inguinal hernia, pyelonephritis

Pathology

- Pathogenesis: Obstruction of the lumen (faecal, tumour, worms) → ↑intraluminal pressure → ischaemia and bacterial invasion → inflammation → ↑oedema
- Macroscopic appearance: congested, dull, fibropurulent exudate on serosa, luminal abscess, gangrene, rupture
- Microscopic appearance: neutrophils in mucosa, submucosa and muscularis propria, necrosis +/- abscess

Treatment

- If not sure, observe: it will get better or worse
- Supportive care: IV, NG, restore hydration
- Appendicectomy
- Metronidazole + cefuroxime (reduce wound infection)

Children

- Anatomic variations:
 - Typical site only 30 – 40% of time
 - PR: pain on right side → retrocaecal appendix (30%). Pain may radiate up right flank. May be no abdominal tenderness
 - Pelvic (23%). If in contact with bladder → sterile pyuria. If in contact with sigmoid → diarrhoea
- Course accelerated:
 - Tiny lumen, ↑inflammation, perforate quickly
 - Dehydration, tachycardia and shock
 - Board-like abdomen *after* resuscitation
- Treatment:
 - Resuscitation first: HG, IV, antibiotics
 - Operate when: ↑urine output, ↓temperature, ↓pulse rate. Anaesthetics → vasodilation and cardiac depression → ↓↓ BP if not well hydrated

Complications

- Wound infection
- Perforation → peritonitis → infertility in girls (⇒ lower threshold for surgery in girls)
- Abscess
- Bowel obstruction (related to perforation → adhesions)

Other Disorders of the Appendix

- Mucocoele of the appendix: dilation of the appendiceal lumen by mucus duct hyperplasia (either benign or malignant)
- Pseudomyxoma peritonei: ‘Jelly Belly’. Mucinous cystadenocarcinoma invading the peritoneum, fills with tenacious semisolid mucus. Treated with serial resection

Ulcerative Colitis (UC)

- = Chronic inflammation of colonic mucosa (only). Unknown aetiology

Epidemiology

- More common than Crohn’s.
- 1 in 1500 in US. Rare in developing countries
- Peak incidence in 25 – 30 year olds
- Smoking is protective
- Risk in 1st degree relatives increases 15-fold
- F > M, W > B

Symptoms & Signs

- Diarrhoea if disease extends above rectosigmoid junction
- Mucus and blood per rectum
- Urgency to defaecate
- Abdominal pain, tenderness
- Relapsing-remitting in 65% patients
- If severe attack: fever, tachycardia, hypoalbuminaemia
- May have: erythema nodosum, arthropathy, aphthous ulcers in mouth and liver complications

Investigations

- Stool culture: exclude infectious
- Bloods: ↑ESR and acute phase proteins
- Possible deficiencies: Fe, Hb, albumin, electrolyte abnormalities
- Sigmoidoscopy: red, raw, granular mucosa
- Colonoscopy & biopsy. Spreads from rectum to some point in colon.

Pathology

- Macroscopic appearance:
 - Begins in rectum and extends in continuity to left colon. 40 – 50% limited to rectosigmoid colon. 10% have pan-colitis, may also develop ‘backwash’ ileitis.

- Mild: Erythema only. Severe: Mucosal haemorrhages and broad-based ulcerations (not deep though). Normal appearance during relapses
- Pseudopolyps: islands of remaining, regenerating mucosa
- Microscopic appearance:
 - Mucosal inflammation only: mucosal ulcers
 - Neutrophils, plasma cells, histiocytes in lamina propria
 - Crypt abscesses (neutrophils in crypt) suggestive of UC rather than Crohn's. May extend into laminar propria to produce ulcers
 - Chronically, mucosa becomes thin and atrophic
 - Distortion of crypt architecture, branching
 - Overtime → dysplasia → flat carcinomas (cf raised in colorectal cancer)

Differential diagnosis

- Microscopic (lymphocytic colitis), Collagenous colitis or Crohn's colitis
- Irradiation proctitis
- Infection, IBS, or Cancer
- CMV or herpes simplex in immunosuppressed patients

Complications

- Anaemia due to chronic blood loss
- Toxic megacolon: diameter of transverse colon > 5.5 cm. Acute dilation of colon due to loss of muscle tone → ↑gas → distension → vascular occlusion → necrosis. May rupture → peritonitis. Emergency
- ↑Risk of colon carcinoma. Key risk facts:
 - How long have they had it (main one): 1% at 10 years, 30% at 30 years. Require regular screening
 - How much bowel is affected: greatest in pancolitis. Minimal with only rectal involvement
 - How well controlled is the inflammation
 - Aggressive flat lesions, infiltrates quickly into lymphatics in submucosa
- Perforation
- Fibromuscular strictures (check to exclude malignancy)

Treatment

- Sulphasalazine +/- steroids (or azathioprine). Need regular FBCs

Crohn's Disease

- = Chronic granulomatous inflammation of the gut

Epidemiology

- Incidence increasing. Peaks in 2nd to 3rd decade
- 1 per 1000 in UK
- F > M, W > B

Symptoms & Signs:

- Malaise, weight loss (65 – 75%), failure to thrive, malabsorption
- Diarrhoea (70 – 90%)
- Rectal bleeding (45%)
- Pain (50%, from inflammation, infection, obstruction, colicky from intermittent obstruction of terminal ileum)
- Perianal disease (50 – 80%)
- Mild fever (30 – 40%)
- Anaemia, glossitis (due to malabsorption)
- Aphthous ulcers in mouth
- Erythema nodosum (painful red nodular lesions on shins), pyoderma gangrenosum (recurring skin ulcers – 10 cm), clubbing
- Asymptomatic periods for weeks-months
- Attacks may be precipitated by emotional/physical stress
- Risk factors: genetic, smoking, high sugar/low fibre

Aetiology

- Type 4 immune reaction: trigger unknown. Cause: ?immune hyper-reactivity

- Proposed agents: viruses, disordered immunologic response to ingested antigen
- Genetic susceptibility. 10-fold risk in first-degree relatives
- ⇒ Multifactorial → abnormal regulation of inflammatory mediators

Investigations

- Bloods: check for anaemia (including anaemia of chronic disease), malabsorption, inflammatory measurements, ↑ESR and acute phase proteins
- Deficiencies: folate, iron, B12, etc, electrolyte abnormalities
- Culture to exclude infective causes
- Sigmoidoscopy/colonoscopy + biopsy
- Upper GI endoscopy
- Barium contrast of small & large bowel: strictures, fistula, cobblestone appearance, skip lesions etc

Differential

- Ileal disease: Tb, Lymphoma
- Colonic disease: colitis (ulcerative, ischaemic, radiation, collagenous), infection (salmonella, shigella, campylobacter), cancer
- Malabsorption: lactose intolerance, coeliac disease

Pathology

- Location:
 - 75% terminal ileum
 - 50% also involves colon
 - 25% colon only (predominantly right side)
 - <5% oesophagus, mouth
- Macroscopic appearance:
 - Skip lesions
 - Transmural inflammation
 - Thickened, inflexible (resembles rubber hose) with narrow lumen
 - Thickened, fibrosed mesentery and enlarged regional lymph nodes
 - Strictures, fistulas, abscesses
 - Mucosa: varying degrees of erythema and oedema. Cobblestone mucosa
- Microscopic appearance:
 - Submucosal and subserosal inflammation with only secondary mucosal involvement (ie glands may be straight, unaffected)
 - Aphthoid ulceration of the mucosa
 - Lymphocytic infiltrate, fibrosis
 - Multifocal granulomatous vasculitis
 - Non-caseating granulomata (only 60%): can have some Langhans/giant cells (horseshoe pattern of nuclei around periphery of a giant cell), but usually granulomas poorly circumscribed

Treatment

- Aim: suppress activity, restore quality of life, prevent complications
- Diet: nutritional supplements. Malnutrition a real risk, → growth retardation in kids. May need enteral or TPN feeding for 'Bowel Rest' → ↓antigen load (controversial)
- Corticosteroids e.g. prednisone: symptomatic relief
- 5-aminosalicylic acids e.g. meizalazine
- Antibiotics (mainly colonic and perianal disease, ↓antigen load): metronidazole
- Steroid sparing immunosuppressives: azathioprine
- Cholestyramine: absorbs bile (normally absorbed in the terminal ileum) to stop it getting into the large bowel, where it causes irritation
- Surgery
- Monitor: inflammatory markers

Complications

- Episcleritis (reddened sclera)
- Stricture, obstruction, fistulas (to bowel, bladder, vagina)
- Malnutrition
- Large & small bowel cancer (5% at 10 years – ie small risk – not screened for)

- Ankylosing Spondylitis
- Pyoderma gangrenosum
- Iritis
- Arthritis

Comparison with Ulcerative Colitis

	Crohn's	Ulcerative Colitis
Macroscopic	Skip lesions Transmural inflammation Thickened wall Often proximal to large bowel Cobblestone appearance	Continuous Mucosa only affected Large bowel only Pseudopolyps
Microscopic	Granulomas (only 60%, poorly formed – pale area with giant cells) Crypt architecture preserved (like a row of soldiers) Muscularis involved	Superficial No granulomas Crypt abscesses Distorted crypt architecture Ulcers
Complications	Minor cancer risk Fistulas, strictures, fissures	Major cancer risk Toxic megacolon
Surgery	Recurs at anastomosis. Surgery for obstruction and abscess common	Colectomy = 'cure'

Small Bowel Tumours

- Benign: Polyps (Peutz-Jeghers), Juvenile Polyps, Adenomas, Stromal tumours
- Malignant:
 - Carcinoid tumours:
 - Tumours arising from neuroendocrine cells
 - Mainly midgut. Similar tumours occur in lungs, ovaries, biliary tree
 - Macroscopic appearance: submucosal elevations, yellow/grey, infiltrative, ulceration, multiple
 - Microscopic appearance: Uniform cells, oval nucleus, fine chromatin, pink cytoplasm, neuroendocrine granules
 - Clinical: malignancy depends on site. Appendix and rectum better, ileal and colonic worse
 - Carcinoid Syndrome: due to excess serotonin. Occurs with hepatic metastases (liver efficiently removes 5HT from portal circulation) → wheezing, right sided heart failure, diarrhoea (↑ motility), abdominal pain, oedema, skin lesions
 - Lymphomas of the GI tract
 - Affects stomach, ileum, colon, jejunum. Arise in the gut, or spread there from elsewhere
 - 3 types: MALT, Sprue associated, and immunoproliferative small intestinal disease
 - Macroscopic appearance: plaque-like expansion of the mucosa → ulcerating, fungating mass, can → obstruction or perforation
 - Microscopic appearance: tumour cells diffusely infiltrate the wall, cytologically resemble follicular lymphoma cells
 - Clinical outcome: prognosis depends on depth of invasion, size, direct extension
 - Adenocarcinoma: Uncommon. Resembles those in the colon

Colorectal Cancer

Presentation

- Change in shape of stools significant (e.g. pencil shaped)
- Rectal bleeding/mucus
- Persistent changes in bowel habit
- Tenesmus: constant feeling of need to defacate, even after passing stool
- Weight loss
- Anaemia
- Abdominal or rectal mass in late presentation
- Hepatomegaly (from secondaries)

- By 75 years, 1 in 20 males and 1 in 25 females (Victoria)

Risk Factors

- Environmental factors: diet, lifestyle, smoking
- Family history
- Premalignant lesions

Family History and Colorectal Cancer

- Average risk = up to two 1st or 2nd degree relatives with bowel cancer at 55 or older (as long as on different sides of family). 98% of population
- Moderate risk = either one 1st degree relative diagnosed before 55 years, or two 1st or 2nd degree relatives on one side of family diagnosed at any age. 1% population. Refer for colonoscopy every 5 years from age 50 or 10 years younger than earliest diagnosis in family
- High risk = more than above, including FAP or identified high-risk mutation in near relative. <1% of population. Suggest genetic testing. Referral to plan appropriate surveillance
- Incidence has been declining since 1950's (5.8% decrease in men, 12.9% decrease in women)
- People may not know family history: can they get death certificates of relatives

Polyps

- = Any lesion which protrudes above the level of the surrounding mucosa
- Hyperplastic polyps
 - 90% of all polyps, measure < 0.5 cm, mainly in rectosigmoid
 - Benign, no premalignant potential
 - "Dew drop" appearance, on top of mucosal fold
 - Sessile (no stalk), often multiple, very common
 - Microscopically: elongated crypts, goblet and absorptive cells, excess mucus
- Adenomatous polyps
 - 10% of polyps
 - Neoplasms: precursors of most colonic carcinomas. Normally removed as don't know which will become invasive
 - Malignancy related to size: <1.5 cm only 1% contains a carcinoma, > 1.5 cm 10% will contain a carcinoma-in-situ. As long as it's confined to the mucosa, there is no metastatic potential. If submucosal invasion then segmental resection
 - Macroscopically: stalk (ie pedunculated)
 - Microscopically: neoplastic glands, hyperchromatic, etc
 - *Tubular adenomas*: Most common (75%), usually pedunculated, most common in left colon, M > F, 50% are solitary, continued colonoscopic follow-up necessary. Head has closely packed tubules/glands lined by non-differentiated neoplastic columnar cells. Stalk has normal colonic mucosa
 - *Villous adenomas*: Papillary projections, larger, more likely to harbour carcinoma, sessile, 10 – 15% of adenomatous polyps, mainly rectosigmoid
 - *Tubulovillous* adenomas: contain 25 – 75% of villous component. May secrete lots of mucus
- Juvenile polyps:
 - Left side of large bowel of kids
 - Cause rectal bleeding
 - Grossly look similar to adenomas
 - Microscopically not neoplastic. Cystically dilated mucous glands, inflammation of lamina propria, maybe ulceration
- Peutz-Jeghers Syndrome: Polyp containing mucus filled cysts and smooth muscle in the lamina propria. No malignant potential. Maybe pigmentation in the mouth
- Polyposis syndromes:
 - Familial Adenomatous Polyposis (FAP): 0.5% of all colorectal cancers. Autosomal dominant, antioncogene mutation of APC gene. APC gene: 1 in 10,000 have mutation → 100s of adenomatous polyps appearing in 2nd or 3rd decade. Will develop carcinoma ⇒ prophylactic colectomy. APC gene also mutated in sporadic cancer
 - Hereditary Non-polyposis Colon Cancer (HNPCC): Aka Lynch Syndrome. 5% of non-FAP colorectal cancers. Patients often young with multiple tumours. 1 – 5 % of all CR cancer. Autosomal dominant – defect of DNA mismatch repair genes – MMR gene (mismatch repair) - 1 in 1,000 have mutation

- Gardner's Syndrome: colonic polyposis, epidermoid cysts (skin), osteoid osteomas (benign bone tumours). High risk of carcinoma
- Turcot's Syndrome: colon polyps + brain tumours

Adenocarcinomas of the Colon

- Epidemiology:
 - In US, 2nd only to lung cancer in cancer deaths. Much lower in third world (\Rightarrow environmental factors)
 - Peak incidence in 7th decade (ie old), except APC and UC
 - 70% in recto-sigmoid colon, rest all the way back to caecum
 - M:F is 2:1 for rectal, equal for right sided
- Aetiology:
 - Adenomatous polyps (esp villous)
 - Ulcerative colitis
 - Familial multiple polyposis
 - Family History
 - Environmental factors: High incidence in Europe/North America, low in Asia/Africa. Urban > rural
 - Diet: High fat and low fibre (slower transit \rightarrow ? \uparrow exposure to carcinogens)
- Pathogenesis: increasing loss of heterozygosity in genes involved in DNA repair, tumour suppression and oncogene activation. Either through \uparrow turnover due to mucosal damage \rightarrow \uparrow risk of gene match failure or directly genotoxic mechanism
- Presentation:
 - Left sided: annular encircling \rightarrow napkin ring or apple core constriction. Signs of obstruction. Poorer prognosis despite earlier detection due to \uparrow invasion
 - Right sided: large fungating or sessile masses, necrotic areas, occult bleeding, anaemia, weight loss
 - May produce mucus, ulceration \rightarrow blood loss
 - Doubling time of about 2 years
- Macroscopic description: Early: may still appear to be a polyp or sessile. Later: obliterate precursor adenoma
- Microscopic appearance: Most are moderately differentiated, irregular glands with pleomorphic cells, usually lack mucus production. Mucinous carcinomas (10 – 15%) have pools of mucus, cleaves through tissue aiding spread (worse prognosis)
- Variants: Adenosquamous carcinoma, small cell undifferentiated (rare), Ulcerative colitis \rightarrow poorly differentiated colitis

Other large bowel tumours (Gastro-intestinal stromal tumours: GIST)

- Carcinoid tumours: most common in appendix and stomach. See Small Bowel Tumours, page 171
- Lymphomas: Non-Hodgkin's. Eg MALT
- Mesenchymal tumours (eg leiomyomas): much less common

Diagnosis

- Rectal exam
- FOBT: sensitivity 50% and low specificity
- Sigmoidoscopy picks up 40% (& take biopsy).
- Colonoscopy: expensive, miss rate for cancer 2-3%
- Double contrast barium enema: cheaper, miss rate for cancer 10 – 15%
- Check for dissemination: LFT, Abdominal CT, CXR (25% have metastatic disease at presentation)

Differential

- Diverticular disease, Inflammatory Bowel Disease, Irritable Bowel Syndrome, Rectal ulcer

Treatment of Colorectal Cancer

- No role for radiotherapy in colon
- Adjuvant chemotherapy:
 - Improves 5 year survival over surgery alone from 50 to 60/65% (but can't predict who will benefit)
 - \uparrow Quality of life (side effects of cancer are pretty severe, chemo reduces these)
 - Given after surgery
 - Six months of 5FU

- Currently given to:
 - Dukes C: All patients (C1 = Muscularis propria + lymph node, C2 = serosa + lymph node)
 - Dukes B2 (serosa): High risk groups, perforation, invasion of adjacent organs, diploid tumours
- Rectal cancer:
 - No serosa around rectum – cancer infiltrates straight into fat – harder to get clear resection margins
 - Radiation in rectal cancer good: but → impaired function and may irradiate small bowel → fibrosis. Try and predict who needs irradiation and do it pre-operatively
- Palliation: hospice + chemotherapy better quality of life than hospice alone

Prognosis of Colorectal Cancer

- Invade into serosal fat, metastasise to regional lymph nodes then to liver and lungs. Rarely intraperitoneal spread
- Complications: Obstruction, perforation, haemorrhage, fistulas
- Prognosis mainly related to stage (how far it's spread), to a lesser extent the grade and location
- Pre-operative staging: ultrasound of liver, Xray of lungs
- Duke's Post-operative staging:

Dukes Stage	5 year survival	Level of Invasion
A	100%	Mucosa
B	60%	Serosal wall but not lymph nodes
C	30%	Lymph nodes
D	5%	Distant Metastasis

- Wgtn Hospital uses APC staging (Australasian Pathologists): minor differences to Dukes
- 5 year survival = cured – unlikely to relapse after that

Follow-up

- Colonoscopy (e.g. initially rest of colon for 2nd primary, then every 3 years)
- Monitor tumour marker CEA (colonic embryonic antigen). Also raised in a variety of other tumours & benign cancers. Not sensitive for early cancers (4% of Duke's A). Neither sensitive nor specific

Diverticular disease of the colon

Aetiology & Epidemiology

- ↓Dietary fibre → ↓stool weight and ↓colonic transit → ↑colonic pressure
- 50% in > 70 years

Symptoms & Signs:

- Most asymptomatic
- Uncomplicated disease (Diverticulosis): non-specific tender sigmoid colon, cramping lower abdominal pain (esp. LIF), altered bowel habit (hard or ribbon like stools, e.g. due to stricture)
- Complicated disease (Diverticulitis): constant pain worse with movement, fever, shock, peritonitis, haemorrhage, guarding, palpable mass, ileus, distension, obstruction (= "Left sided appendicitis")
- PR bleeding not usually concurrent with guarding

Pathology

- Diverticulosis: multiple out-pouchings or herniations (= diverticula) of the mucosa through the muscle wall of the bowel at the point where arteries penetrate the bowel wall
- Diverticulitis: inflammation of the diverticulum caused by obstruction of the neck, faecal impaction, constricted blood supply, infection from luminal flora
- Complications:
 - Abscesses → obstruction, bleeding due to erosion of blood vessels
 - Stricture from scarring

Investigations

- Bloods usually normal in uncomplicated disease: do FBC and LFT
- Complicated disease: inflammatory/infection markers (eg blood cultures if temp > 38 C)
- CT, ultrasound, colonoscopy
- Contrast enema one month later (never acutely – risk of perforation) to confirm diverticulum and exclude cancer

Differential

- Cancer
- Inflammatory bowel disease
- Drug induced colonic symptoms
- Abscess/perforation: pyelonephritis, perforated peptic ulcer, ischaemic colitis
- Haemorrhage: polyp, angiodysplasia, GI bleeding
- Stricture: radiation damage, ischaemic colitis, endometriosis
- Malabsorption: lactose intolerance, coeliac disease
- Infection: campylobacter, other infection

Treatment:

- Acute management:
 - Fluids (nil by mouth to rest gut)
 - For diverticulitis: antibiotics (eg cefuroxime and Metronidazole. If really nasty then Gentamycin, Amoxycillin and Metronidazole)
 - Epidural would be good for pain but is contraindicated if risk of sepsis
 - Usually settles with conservative management. If not, then resect affected colon:
 - Hartman's procedure: Remove affected segment. Bring proximal bowel out to a colonostomy. Temporarily close off distal segment
 - Reverse colonostomy 3 months later
- Chronic management:
 - ↑Fibre, ↑fluids, ↑exercise
 - For constipation: bulking agents, lactulose
 - For pain relief: anticholinergics (cyclosporine), antispasmodics

Irritable Bowel Syndrome (IBS)

- Very common (up to 15 – 20%)
- F > M

Symptoms & Signs

- Crampy lower abdominal pain relieved by defaecation or flatus, associated with change in stool frequency/consistency
- Diarrhoea (rarely at night) and mucus
- Distension, variable abdominal tenderness
- Nausea, heartburn, early satiety
- Urinary frequency
- Exacerbated by anxiety or stress
- Age < 50 years
- Feeling of incomplete evacuation
- But NO blood, weight loss or recent onset

Diagnosis

- A diagnosis of exclusion
- Continuous or recurrent symptoms for at least 3 months
- Abdominal pain relieved by defecation or associated with a change in bowel habit
- Irregular pattern 25% of time with 2 or more of:
 - Change in frequency (> 3 per day or < 3 per week)
 - Change in form (lumpy/hard/loose)
 - Change in passage (straining/urgency/feeling of incomplete evacuation)
 - Mucus
 - Bloating/distension

Investigations

- Exclude other conditions, e.g.:
 - FBC: anaemia and nutritional deficiency
 - LFT: exclude biliary colic
 - Thyroid function: exclude myxoedema (→ constipation) or thyrotoxicosis (→ diarrhoea)
 - Colonic imaging for new or different symptoms in > 40 years – exclude cancer/IBD
 - Faecal fat, breath test, lactose tolerance test

Differential

- Diagnosis of exclusion, so the differential is everything else
- Cancer, IBD, diverticular/ceeliac disease, infection, diverticular disease, chronic pancreatitis, biliary/liver disease, peptic ulcer, motility disorder, bacterial overgrowth, laxative abuse, endometriosis, ovarian malignancy, thyroid disease

Aetiology

- Abnormal gut motility
- Enhanced visceral sensitivity
- Psychological/psychiatric disorder
- Food allergy/intolerance

Treatment

- Supportive, reassurance, stress reduction, ↑ fibre (RDA = 25 – 30 grams, average is 15), ↑ fluids (2 litres per day), ↑ exercise
- For constipation: bulking agents, lactulose
- For pain relief: anticholinergics (cyclosporine), antispasmodics
- For confirmed diarrhoea: antimotility drugs (loperamide, codeine phosphate)
- If depressed then antidepressants

Bacterial Overgrowth of Small Intestine

- =Aerobic G+ bacteria replaced by anaerobic G-, esp. E coli & clostridium difficile (toxin causes diarrhoea) often in a blind loop of bowel, or in the small bowel which usually has low bacterial load
- Symptoms & Signs:
 - Diarrhoea, abdominal pain, weight loss
 - Steatorrhoea, anaemia, ataxia/neuropathy (due to B12 deficiency – bacteria eat it all)
- Investigations:
 - Blood: check for anaemia, B12, folate
 - Schilling test
 - Stool fat
 - Barium x-ray for jejunal stricture/diverticulitis, ↓motility
 - Duodenal aspiration and biopsy
- Differential:
 - Coeliac disease
 - Chronic pancreatitis
 - Crohn's disease
 - Infections: campylobacter, Giardia, AIDS enteropathy
 - Breath tests: ↑H₂ after lactulose, etc
- Aetiology
 - Motility disorders
 - ↑Bacteria: e.g. ↓stomach acid (hypochlorhydria)
 - Impaired immunity
- Treatment:
 - High protein diet, vitamin supplementation, stop antibiotics
 - Antibiotics: Metronidazole 400 mg TD, Ciprofloxacin 500 mg BD, or vancomycin

Pseudomembranous Colitis

- Acute diarrhoeal illness following broad-spectrum antibiotics
- Overgrowth of clostridium difficile
- Macroscopic appearance: Puss erupting from glands (like little volcanoes, cauliflowers)
- Microscopic appearance: superficial necrosis of epithelium and crypts, ↑↑mucus/puss over the surface

Diarrhoea – Infectious Agents

- = Acute Enterocolitis
- Symptoms & Signs:
 - Dysphagia (e.g. Candida)
 - Flatulence, colic, distension, diarrhoea (watery, fatty, bloody)
 - Vomiting, fever

- Investigations
 - Blood: eosinophilia, HIV
 - Faecal microscopy, parasitology, culture
 - H₂ breath test
 - Endoscopy/Colonoscopy +/- biopsy
- Pathology: Red, oedematous bowel (all look the same), microscopically non-specific inflammation
- Differential
 - Drug induced diarrhoea: laxatives, magnesium compounds, diuretics
 - Severe alcohol intake
 - Diabetic autonomic neuropathy
 - IBD
 - Malabsorption: coeliac, lactose intolerance, lymphoma, pancreatitis, biliary/liver disease
- Management:
 - Rehydration
 - Investigate cause
 - Monitor complications: anaemia (due to haemorrhage), septicaemia, perforation, appendicitis
 - Strict food hygiene
 - Avoid milk → ↓secondary hypolactasia
 - Antibiotic treatment

Infectious agents

- Bacterial enteroinvasive:
 - *Campylobacter Jejuni*
 - Poultry
 - Haemorrhagic colitis
 - Erythromycin (used to be ciprofloxacin but it's been put in chicken feed → ↑resistance)
 - *Escherichia Coli*
 - Enterotoxic subspecies
 - Travellers diarrhoea
 - *Salmonella/Shigella*: Poultry
- Bacterial enterotoxins:
 - *Vibrio Cholerae*
 - *Staph Aureus*: Food poisoning (eg cream buns)
 - *Clostridium Botulinum*
 - Some subtypes of *E Coli*
- Protozoa
 - *Giardia*
 - Trophozoites reside mainly in duodenum, also small bowel
 - Cysts in faeces
 - Small bowel diarrhoea → diarrhoea during night (large bowel ‘sleeps’)
 - *Entamoeba histolytica*: causes amoebic dysentery (colitis)
- *Cryptosporidium*
 - Common in kids
 - Is chronic in immunocompromised
 - No effective antibiotic treatment

Constipation

- = Infrequent bowel action (ie > 3 days) or difficult/painful defecation
- Affects 3% in young adults → 20% in elderly
- Physiology:
 - Muscular movements: segmentation mixes bowel contents. Peristalsis moves it along. Mass movements occur once or twice a day (usually after a meal)
 - Faecal mass in rectum → internal anal sphincter opens by reflex. External sphincter remains contracted voluntarily, but will tire quickly → leakage
 - Defaecation requires relaxation of external sphincter, pelvic floor muscles and abdominal straining
 - Motility affected by sympathetic (→ ↑segmentation) and parasympathetic (→ ↑peristaltic and mass movement) system, hormones, fibre, acid pH, lactobacilli
 - Age related changes: mucosal atrophy (→ ↓mucus), muscular atrophy, etc

- Assessment:
 - History: What do they mean? Frequency, stool consistency, presence of blood/mucus, ease of evacuation, onset of symptoms, and drug history.
 - In elderly screen for risk factors: ↓fibre following changed diet or false teeth, can't shop or prepare food, ↓physical activity → ↓transit time, dehydration, neurological disease (eg diabetic neuropathy)
 - Exam: systemic disease, abdominal exam and perianal sensation
 - Investigations: Usual, plus blood tests to exclude anaemia, hypothyroidism and electrolyte abnormality
- Management:
 - Review medication, eg:
 - Opioids
 - Anticholinergics (eg antihistamine, antiemetics)
 - NSAIDS
 - Serotonin antagonists
 - Phenothiazines
 - Tricyclic antidepressants
 - Bowel retraining. Try during high motility periods – first thing in the morning and after meals. Exercise to improve abdominal muscles
 - Adequate fibre and fluid
 - Laxatives:
 - Hydrophilic bulk forming agents, eg Normacol, Metamucil. Must also take adequate water. Not useful in palliative care (patients are too sick to eat it)
 - Osmotic agents, eg lactulose or sorbitol → not broken down in small bowel → ↑osmotic gradient → ↑water content. Take 1 to 2 days to act. Safest agent in the long term
 - Stool softeners and lubricants. Take 1 to 3 days to act. Act as detergents top increase water penetration and thus softening of the stool. Eg docusate agents, Coloxyl (a detergent effect → breaks up stool, may be hepatotoxic) and lubricants. Oil based lubricants (eg paraffin) can affect vitamin and drug absorption and be aspirated
 - Stimulants and irritants → ↑peristalsis and net fluid secretion. Eg Senna. Take 6 to 12 hours to act. Stimulates the myenteric plexuses to produce peristalsis. Avoid irritant laxatives unless impaction, severe muscle weakness. Long term use of laxatives causes constipation by damaging the nerve supply of the gut
 - Locally acting agents eg glycerol suppository at peak motility time. Can have osmotic and irritant agents
 - Investigational agents such as cisapride (prokinetic agent)
 - Rectal Laxatives:
 - For faecal impaction
 - On exam will either have a loaded rectum or ballooning of the rectum (dilated distally ⇒ impacted further up)
 - Types:
 - Glycerine suppositories: soften stool by lubrication and osmosis
 - Bisacodyl (Dulcolax) suppositories: Causes peristalsis
 - Sodium Phosphate enemas
 - Oil Enemas

Fibre

- Dietary Fibre: the undigested and unabsorbed polysaccharide (cereal, fruit, vegetable) that remains at the end of the small bowel. Contains cellulose and non-cellulose polysaccharides, lignin, gums and waxes
- Worth a trial in constipation, IBS (esp. with constipation) and non-ulcer dyspepsia of dysmotility type
- Get good 24 hour dietary history
- Intake from cereal source is 4 or 5 times greater than fruit or vegetables. It is also less fermented in large bowel
- Ideal level = 30g/24 hours. Usual NZ adult approx. 15 g/24 hours
- 20 g of fibre in 6 tablespoons of bran, 2 Weetbix or 4 large thick slices of whole meal bread
- Suggestions for use:
 - Increase SLOWLY (i.e. aim for a full bowl of All bran in 2-3 months): otherwise bloating, distension, gas

- Take fibre every day
- Necessary amount is not a weight – but the amount necessary to keep stools soft
- Drink lots of water (2 L per day is recommended)
- Will increase gas (fibre promotes bacterial growth): take stairs not lift!

Other Bowel Diseases

- Collagenous colitis:
 - Chronic or episodic watery diarrhoea
 - F > M, 30 + years, autoimmune association
 - Macroscopic appearance: Looks normal at colonoscopy
 - Microscopic appearance: subepithelial hypocellular collagen band (prevents H₂O absorption)

Anorectal problems

- Haemorrhoids:
 - Dilated veins beneath the submucosa. Bleeding from overlying mucosa
 - Don't cause pain unless prolapsed or thrombosed
 - Can cause Pruritis ani
 - Treatment: injection with injected sclerosant (eg almond oil), banding (but infection and bleeding risk), infra-red coagulation
- Rectal Prolapse:
 - Self-limiting in kids, in elderly due to weakened pelvic floor (childbirth or denervation)
 - Treatment is surgical, faecal incontinence improved in half
- Rectal Cancer:
 - Majority can be felt on digital examination
 - Adenocarcinomas
 - Presentation: bleeding and tenesmus, rarely pain
 - Treatment: local excision or resection
- Fissures:
 - Vertical tear in anoderm. 90% posteriorly
 - Acute or chronic
 - Vicious circle: tight internal anal sphincter → tear → reflect spasm → constipation etc.
 - History: severe pain and bleeding on defaecation
 - Associated with high resting anal pressure
 - Treatment: High fibre diet, lots of H₂O, local analgesic cream, GTN paste (relaxes sphincter) (all conservative), limited internal sphincterotomy
- Abscesses and fistulae:
 - Infection of tiny glands emptying at dentate line.
 - Infection can burrow into perianal fat or ischiorectal fat
 - Drainage may result in anal fistula
- Pruritis Ani (itchy anus):
 - Usually worse at night
 - Causes by anal or dermatological conditions
 - Anal: haemorrhoids, keyhole deformity, pinworm infection, anal warts and cancers
 - Dermatological: Bowen's disease, Paget's disease of anus, eczema
 - Treatment: avoiding strong steroid creams, avoiding itching, and drying carefully
- Anal warts: Condylomata acuminata. Caused by HPV 8 and 11. Usually an STD
- Anal Cancer: Uncommon. Spreads to inguinal glands. Can be adenocarcinoma, basaloid carcinoma (this and next two caused by HPV 16 and 18), squamous carcinoma, muco-epidermoid carcinoma, anal melanoma.
- Perianal suppuration
- Angiodysplasia (submucosal proliferation of vessels – associated with age and aortic stenosis)
- Anal cancer (rare): related to HPV (as with cervical cancer) → anal intraepithelial neoplasia. Risk factors as for cervical cancer (number of partners, age of first intercourse, etc). Above dentate line – endodermal origin → adenocarcinoma. Below dentate line – ectodermal origin → squamous or basal cell carcinoma or melanoma

GI Bleeding

Upper GI Haemorrhage

- Symptoms/Signs:
 - Haematemesis (either fresh or coffee ground appearance): check not coughing it up. Can check vomit with urine dipstick for blood
 - Melena (black/sticky foul smelling stools): stomach denatures haemoglobin → black. So no melena if bleed beyond proximal small bowel. Exclude iron tablets, bismuth preparations & Guinness
 - Rectal bleeding (haematochezia)
 - Anaemia: tired, pale, breathless, faint (brain struggles to compensate if PO₂ <60 mmHg)
 - Hypovolaemia: carotid bodies → sympathetic → ↑HR & peripheral vasoconstriction; ↓renal perfusion → ↑renin → ↑angiotensin (vasoconstriction) → ↑aldosterone (H₂O retention); ↑ADH → thirst and H₂O retention. If serious hypovolaemia: postural hypotension, cold & clammy, confused, thirsty, weak pulse & tachycardic, ↓urine output
 - Check stridor: tumour compressing trachea – expiratory wheeze
- History:
 - Always ask about CV and respiratory history, and when they last ate, in case surgery is needed
 - Medications: NSAIDs (if so, then steroids further increase risk), anticoagulants
- Investigations:
 - Bloods: anaemia, reticulocytes, group & hold, U &Es, Liver fn (is it varices?), clotting (either poor liver function or Warfarin → bleeding)
 - Endoscopy (can do biopsy)
 - Barium swallow (not so good)
- Causes: Tear, varices (check splenomegaly, spider naevi, palmar erythema, risk of death 30%, risk of rebleed, 30%), oesophagitis (e.g. from reflux or ulcer), Mallory-Weiss tear from repeated vomiting, gastritis (e.g. alcoholic), ulcer, malignancy (check for masses, lymph gland enlargement, organomegaly), ulcer (NSAIDs)
- Causes of small bowel bleeding (eg if no upper or lower cause found):
 - Under 25: Meckel's diverticulum
 - 30 – 50: Small bowel tumour
 - Over 50: angiodysplasia

Lower GI Haemorrhage

- Symptoms/Signs:
 - Blood in/with stool. Colour indicates site: if bright red ⇒ 95% of pathology distal to splenic flexure (usually anus & rectum)
 - Pain on passing motions ⇒ anal fissure (haemorrhoids don't cause pain unless prolapsed)
 - Anaemia
 - Angina (in elderly with CHF, anaemia → angina due to ↓O₂ → ↑heart work)
 - Check: Meikels diverticulum – lined with gastric mucosa
- Family Hx: colorectal cancer/inflammatory bowel disease
- Rectal Exam (Always do abdominal exam as well)
 - Look first: skin tags ⇒ Crohn's, sentinel tags ⇒ chronic anal fissure
 - Digital examination: if acute fissure this will be very painful (⇒ give up)
 - Rigid sigmoidoscope: in 2/3 can only see rectum
- Investigations: rectal exam, sigmoidoscopy, colonoscopy, barium enema, bloods (anaemia, reticulocytes)
- Causes:
 - Diverticular disease (brisk bleeding with sudden onset)
 - Inflammation (ulcerative colitis, etc)
 - Infection (e.g. campylobacter)
 - Colorectal cancer
 - Angiodysplasia
 - Haemorrhoids (blood coats bowel motion with drops after motion passed)
 - Anal Fissure (pain passing motion)
 - Anal Cancer
 - Upper GI bleeding (check with an NG aspirate)

Treatment of Major GI Haemorrhage

- Resuscitate:
 - Colloid drip (expand vascular volume – not crystalloid – that shifts into interstitial space, 14 or 16 gauge)
 - If meet any of the criteria for shock then transfer to ICU: postural hypotension > 15 mmHg fall, tachycardia > 100, systolic BP < 100.
 - Check thirst/urine output (insert catheter)
 - Max O₂
- Bloods: group and hold (don't match until sure you need it), ABG, Hb, baseline creatinine before renal failure, ↑urea – may be due to breakdown of blood in gut, check platelets, INR & APTT for liver disease, bleeding disorders, warfarin OD)
- Find cause:
 - ANY melaena → upper GI down to proximal small bowel
 - Endoscope for upper:
 - Don't endoscope until resuscitated – but do it early. If they rebleed and surgery is required, the surgeon will want to know where its from
 - Endoscope for varices → injection sclerotherapy (e.g. ethanolamine oleate), balloon tamponade
 - For lower bleeding:
 - Sigmoidoscope: check no mass
 - Colonoscopy
 - If pain → ischaemic colitis
 - If aortic surgery → aorticduodenal fistula
 - If not stopping, either labelled red cell scan (view with gamma camera) or mesenteric angiogram (contrast via femoral artery into mesenteric arteries) to guide surgery. These only detect active bleeding
- 65% will spontaneously stop → resuscitate/transfuse and investigate less urgently
- Indications for surgery:
 - Failure of conservative treatment
 - In shock, rebleed, etc
 - Consider if > 6 units of blood needed over 24 – 48 hours

Liver Disease

- NB: This section combines notes from the Gut run, and from Microbiology and Chemical Pathology

Assessment

Presentation

- Found coincidentally when clinically well (e.g. medicals)
- Family screening e.g. abnormal irons, HBV
- Non-specific illness and found to have abnormal LFT: ?alcohol, medicines, viral, jaundice, liver/biliary disease
- Is it acute, chronic, acute on chronic, or a failing chronic

Aetiology

- Acute hepatitis:
 - Viral: A, B, C, D, others
 - Toxic:
 - Drugs
 - Poisoning (eg alcohol)
- Chronic hepatitis:
 - Viral: B, C, B + D, CMV
 - Toxic:
 - Drugs
 - Chronic Alcohol
 - Autoimmune
 - Metabolic:
 - Alpha-1-antitrypsin

- Wilson's disease
- Haemochromatosis
- Fatty liver: Obesity, NIDDM, Drugs, alcohol

History

- Surgery: e.g. cholecystectomy
- Heart disease: congestive heart failure
- Pregnancy
- HIV positive, sexual orientation
- Contact with hepatitis: family, sexual
- Travel: malaria, parasites
- Hepatitis infection risk: Tattoos, body piercing, health care worker, transfusion, IVDU
- Alcohol → acute alcoholic hepatitis
- Ethnic group
- *Medications – ALWAYS ASK ABOUT DRUGS*
- Family History: e.g. anaemias, Gilbert's syndrome, haemochromatosis, gallstones, alcoholism, autoimmune disease, Wilson's disease (copper)
- Symptoms: itch, urine and stool colour

Liver Function Tests (LFTs)

- Investigations:
 - Bloods:
 - Bilirubin
 - LFT: AST, ALT, ALP, GGT
 - Total protein, albumin
 - Tests can be widely variable for the same condition
 - Other: Coagulation studies, ammonia
 - Special tests: α_1 antitrypsin, α_1 feta protein, hepatitis markers, specific autoantibodies, IgG, caeruloplasmin
 - Any liver disorder may → ↑ ferritin (also an acute phase protein)
 - Also test for other causes of liver disease: HBV, HIV, iron studies (ferritin), immune liver disease (\uparrow Anti-nuclear Antibodies – ANA)
 - Imaging: ultrasound +/- CT, MRCP, ERCP. Ultrasound and CT have high false negatives for biliary
 - Percutaneous transhepatic cholangiogram – PCT
 - Liver biopsy the gold standard
- Aim to decide if liver disease is present, is progressing or is severe

Aiming to answer three questions:

- 1) Is there liver cell death – inflammation and hepatonecrosis? Check:
 - Bilirubin: in acute hepatitis will be 50:50 direct and indirect
 - Raised aminotransferases predominate. If AST > ALT think severe cirrhosis, liver malignancy, alcohol. In normal hepatitis ALT > AST
 - Common liver causes:
 - Non-alcoholic steatohepatitis (fatty liver): probably the most common cause of mildly elevated LFTs, especially if obese, Type 2 diabetes and hyperlipidaemia
 - Acute/chronic viral hepatitis
 - Genetic haemochromatosis
 - Autoimmune hepatitis
 - Less commonly: α_1 antitrypsin deficiency and Wilson's disease
 - Causes of abnormal LFTs other than Liver disease:
 - Diseases of other organs affecting liver, e.g. RA
 - Medicines, alcohol, tonics, remedies, poisons
 - Congestive heart failure → hepatic congestion
 - AST: also produced by:
 - Muscle: If normal ALT and ↑AST then do a CK for muscle breakdown
 - Blood: Haemolysis

- 2) Is there cholestasis (=impaired bile flow)? Liver can remove 5 * normal bilirubin from circulation (i.e. large functional reserve). Cholestasis usually refers to obstruction within the liver. ‘Obstructive Jaundice’ ⇒ major ducts. Bile salts are 90% reabsorbed in the terminal ileum. They emulsify fats. Bile also contains cholesterol, phospholipids and bilirubin (reabsorbed → urobilinogen → urine)
- If left or right hepatic duct blocked, other side of liver will be sufficient to keep bilirubin normal
 - GGT released in inflammation: usually in parallel with ALP in obstruction. If ↑GGT and ↑ALP then ALP is from the biliary tree
 - Raised ALP and GGT predominate in cholestatic diseases
 - Common:
 - Biliary obstruction: gallstones
 - Drug hepatotoxicity
 - Neoplasms (eg head of pancreas)
 - Less Common:
 - Primary biliary cirrhosis
 - Primary sclerosing cholangitis
 - Sarcoidosis
 - Autoimmune cholangiopathy
 - Other causes of ↑ALP:
 - ALP from bone and cholangiocytes (biliary epithelium). Excreted in urine, but saturated kinetics → ↑serum level
 - Physiological:
 - Bone: Growth and fractures. High in puberty
 - Pregnancy (placental)
 - Benign ↑ with age
 - Bone disease: Paget’s, malignancy, renal failure, hyperparathyroidism, Rickets
 - GI tract can also produce ALP, eg Crohn’s
 - Miscellaneous: hyperthyroidism, familial benign, transient of infancy
 - GGT ↑ benignly with age and obesity
 -
- 3) Is liver function normal? Are detoxification, synthesis, and glucose management working? Has a large functional reserve. Check:
- Bilirubin
 - Albumin. See below
 - Prothrombin time (INR): factors 2, 5, 7, 9, 10. Give parenteral Vitamin K to differentiate between malabsorption or poor liver function
 - Tests in cirrhosis
 - Liver function tests very variable:
 - Quiescent phase: normal or minor ↑ in LFT
 - Active Phase: ↑ in ALT and AST when necrosis is dominant
 - Causes: idiopathic, alcohol, chronic active hepatitis, primary biliary cirrhosis, haemochromatosis, Wilson’s disease, α1 antitrypsin deficiency
 - Other examples of Liver Function tests:
 - ↑↑ALT and ↑↑AST: viral hepatitis, Paracetamol OD
 - ↑ALP and ↑bilirubin in a 12 year old with vomiting: Gilbert’s syndrome (↑bilirubin when fasting), ALP normally raised at this age
 - ↑Bilirubin, ↑ALP, ↓Albumin + neuro signs → ?Wilson’s disease (very rare)
 - ↑Bilirubin, ↑ALP, ↓Albumin + abnormal electrophoresis → ? ↓α1 antitrypsin

Total Protein

- Normal Ranges:

Total Protein	60 – 80
Albumin	34 – 46
Globulin Gap	~ 20
- Examples:
 - 55 year old man, ↓albumin, normal protein ⇒ ↑Ig (common in cirrhosis)
 - 14 year old, ↑cholesterol, ↓protein, ↓albumin ⇒ nephrotic syndrome (relevance of high cholesterol not understood)

- 58 year old man with diabetes, protein 94, albumin 56 \Rightarrow dehydration (don't get albumin > 50 without dehydration)
- 40 year old post-op, protein 26, albumin 11 \Rightarrow dilution. Took blood downstream of iv line
- 46 year old, enlarged nodes, protein 50, albumin 33 $\Rightarrow \downarrow$ globulin gap \Rightarrow ? immunocompromised/lymphoma
- 60 year old, pneumonia, protein 70, albumin 22 \Rightarrow acute phase + maybe \uparrow Ig
- 50 year old, recurrent abdominal pain, protein 55, albumin 27 \Rightarrow pancreatitis \rightarrow malabsorption
- 38 year old, SOB, rash, protein 86, albumin 34 \Rightarrow sarcoidosis or SLE
- Differentials:
 - Hypoproteinaemia:
 - Haemodilution: poor iv therapy, drip arm, SIADH, pregnancy
 - \downarrow Albumin: \downarrow synthesis (liver disease, malabsorption, malnutrition), losses (renal, gut, skin), non-specific (eg illness)
 - \downarrow Ig: primary or secondary immunodeficiencies. Only IgG deficiency is enough to show up as low protein or on electrophoresis
 - Hyperproteinaemia:
 - Haemoconcentration: dehydration, haemostasis
 - \uparrow Ig:
 - Monoclonal: myeloma, lymphoma, macroglobulin, MGUS
 - Polyclonal: liver disease, infection, autoimmune, sarcoidosis
 - Oligoclonal

Aside: Electrophoresis

- Bands: albumin, α_1 antitrypsin, haptoglobins (α_2 band), transferrin, complement, Ig's
- Two indications:
 - α_1 antitrypsin deficiency
 - Monoclonal antibody band
- Monoclonal Gammaglobulinaemia of Uncertain Significance (MGUS)
 - Benign, but potential for malignant transformation (eg to Myeloma): 5% at 5 years, 25% at 15 years
 - \Rightarrow need to follow up over time
 - See Aside: Conditions associated with Monoclonal proteins, page 303

Causes of Jaundice

- For neonatal jaundice, see Jaundice, page 595
- Unconjugated hyperbilirubinaemia
 - Overproduction: Intravascular or extrahepatic haemolysis
 - \downarrow Hepatocellular uptake: drugs, sepsis, starvation
 - \downarrow Hepatocellular conjugation: Gilbert's syndrome, neonatal jaundice, drugs, diffuse hepatic disease
- Conjugated bilirubinaemia (cholestatic jaundice)
 - Impaired hepatocellular secretion: various syndromes, duct stricture, biliary cirrhosis, steroids
 - Hepatocellular cholestasis – impaired secretion plus liver injury as well: viral infection, drugs, alcohol
 - Extrahepatic obstruction: stones, carcinoma, strictures and congenital atresia

Pathology

- Normal histology:
 - Chords of hepatocytes between sinuses running from portal tract to central vein
 - Zone 3 (perivenular) more sensitive (eg to drugs) than zone 1 (periportal)
- Acute Hepatitis:
 - =Inflammation of the liver: no cause implied
 - Macroscopic appearance: mildly enlarged, tender liver. Flu like symptoms. Jaundice, itching
 - Microscopic appearance:
 - Diffuse liver cell injury with lobular disarray: loss of normal radial array
 - Focal necrosis of hepatocytes with hepatocyte regeneration (mitotic figures, variation in cell size)
 - Portal inflammation: lymphocytes & macrophages. Eosinophils with drugs
 - Bile stasis: variable (often absent), due to disruption of canaliculi, greenish
 - NO fibrosis

- Chronic hepatitis:
 - If longer than 6 months then chronic – otherwise acute (unless chronic signs – e.g. spider naevi)
 - Chronic active and chronic persistent hepatitis reflect different disease activity but caused by the same agents
 - Chronic persistent hepatitis: Benign and self-limiting, following acute hepatitis and lasting several years. Inflammation limited to portal triad (lymphocytes, macrophages and plasma cells). Architecture preserved, no fibrosis, no hepatocyte necrosis
 - Chronic active hepatitis:
 - Progressive hepatic necrosis and fibrosis, potentially leading to cirrhosis
 - Clinical course variable. 5 year survival 25 – 50%
 - Marked portal inflammation extending into lobules
 - Piecemeal necrosis: ‘nibbling away’ at hepatocytes around portal track by lymphocytes → necrosis
 - Bridging necrosis: creating portal-central or portal-portal tracts
 - Hepatitis B: ground glass hepatocytes – large, uniform cytoplasm filled with viral protein
 - Hepatitis C: fatty degeneration, bile duct lesions and lymphoid follicles
- Fulminant Hepatitis:
 - Very rare. Onset to death in 2 – 3 weeks (massive necrosis) to 3 months (submassive failure)
 - Causes: Viral (60%), drugs/chemicals (30%, eg paracetamol poisoning), numerous other minor causes
 - Macroscopic appearance: all/most of liver destroyed. Red, limp, wrinkled capsule. Mushy red
 - Microscopic appearance: Zonal (2,3) or complete necrosis, liquefaction of hepatocytes, little inflammation

Management of Acute Hepatitis

- Avoid strenuous physical activity while jaundiced, increase slowly afterwards
- Best rest only if unwell
- No corticosteroids
- Perhaps reduce fat, abstinence from alcohol
- Care with personal hygiene
- Follow liver tests until normal

Progression of Chronic Hepatitis

- Acute hepatitis (inflammation/cell death) → regeneration → resolution **or** chronic hepatitis, which may → fibrosis (the necessary step for progression to liver failure) → disordered architecture → cirrhosis
- Assessing Liver Biopsy:
 - Is there inflammation around the portal tract? ‘Limiting plate’ surrounds portal tract. Monocytes migrate through this and cause *piecemeal* or *interface* hepatitis. If it extends to another portal tract then called *bridging* necrosis
 - Is there inflammation/necrosis out in the lobule ⇒ intralobular or focal necrosis
 - Are there inflammatory cells in the portal tract ⇒ portal inflammation
 - How much scar tissue/fibrosis is there?
 - Knodell index scores each of these to generate a Hepatitis Activity Index (HAI). Score out of 22
- Child-Pugh Classification of liver function/failure: sum of scores for encephalopathy, ascites, bilirubin, albumin, INR, nutrition

	Score	5 year survival
Grade A	<= 6	50%
Grade B	7 – 9	20%
Grade C	> 9	Few

Alcoholic Liver Disease

- *Alcoholic Steatosis (Fatty Liver):*
 - Pathogenesis: ↑synthesis of TAGs + ↓fatty acid oxidation + ↓formation/release of lipoproteins → fat in lymphocytes
 - Macroscopic appearance: large, pale, liver with soft greasy cut surface
 - Microscopic appearance: Micro and macro-vesicular types. Intracytoplasmic droplets coalescing to fill the cell, may rupture (no inflammation before rupture). Perivenular fibrosis

- Outcome: Liver function may be normal. If no fibrosis then can be cleared
- Fatty liver can also be caused by toxic, metabolic and hypoxic conditions, and occurs in malnourished kids in the third world
- *Alcoholic hepatitis:*
 - Acutely following heavy drinking
 - Often superimposed on fatty change or cirrhosis
 - Microscopic appearance:
 - Similar to viral hepatitis
 - Liver cell necrosis and inflammatory infiltrate
 - Mallory bodies (alcoholic hyaline): intracytoplasmic collection of cyto-skeletal proteins. Looks like candy floss
 - Fibrosis
- *Alcoholic Cirrhosis:*
 - Causes 60 – 70% of cirrhosis. Most of the rest is viral
 - Only 10% of alcoholics get cirrhosis
 - Requires daily alcohol of > 60 gm (1/3 bottle of spirits)
 - Macroscopic appearance:
 - Initially large, fatty, micronodular (liver cells regenerating between fibrosis)
 - Progresses to small, non-fatty, macronodular (>10 mm) liver. Often micro-macro nodular presentation
 - Microscopic appearance:
 - Early: delicate portal-central fibrosis, fatty parenchyma.
 - Late: enlarged nodules surrounded by broad fibrous bands (with signs of liver failure). Bile retention within nodules
 - Immediate causes of death: hepatic coma, GI bleed, infection, hepatocellular carcinoma, head injury → subdural haematoma
 - Alcohol also → pancreatitis (see Pancreas, page 197)

Viral Hepatitis

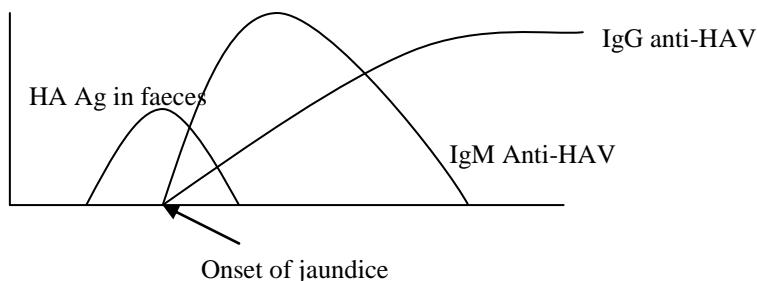
- Causes:
 - Prime target is the liver: Hep A, B, C, D, E,
 - May affect liver secondarily: EVB and CMV
- Distribution of cause of acute hepatitis (e.g. ALT > 1000) in Auckland: A - 25%, B - 25%, EBV - 25%, C - 5 – 10%, some CMV
- Clinical course: variable – from asymptomatic to fulminant/fatal. Common symptoms:
 - Malaise, weakness, lethargy
 - Flu like illness: tiredness, fever, myalgia
 - Anorexia, nausea, vomiting (especially Hep A)
 - Jaundice (uncommon)

	Hep A	Hep B	Hep C
Incubation	2 – 8 weeks (ave 4)	4 – 17 weeks (ave 6)	3 – 20 weeks (ave 7)
Symptoms	20 – 40%	40 – 60%	Mild
Onset	Abrupt	Insidious	
Duration	1 – 3 weeks	1 – 4 weeks, sporadic	
Icterus (Jaundice)	30 – 35%	30 – 40%	10 %
Route of Infection	Faecal/oral	Parenteral/sexual	Blood
Chronic infection	None	10 – 15%	50 – 80%
Mortality	0.05 – 0.1%	1 – 2%	
Diagnosis	IgM anti-HAV IgG anti-HAV	IgM Anti-HBc, HBsAg, HBeAg	Exclusion. After 3 months Anti HVC. HVC RNA PCR earlier
Vaccination	Havrix: 99% cover	Engerix B: 90 – 95% cover	None

Hepatitis A

- = Infectious hepatitis
- 25 – 33% of clinical cases of hepatitis
- Especially in kids, normally mild

- Transmitted by food (especially raw shell fish) or contaminated water.
- Decreasing over time due to ↑ hygiene and good vaccine
- Viraemia lasts 7 days after onset of jaundice. Don't get virus in the blood (or only transiently). It's a gut bug
- Symptoms: arthralgia, weight loss, fatigue, low grade fever, loss of appetite, abdominal pain
- Diagnosed by IGM Anti HAV & ?exclusion of HBV
- Treatment: supportive, dietary restriction, rest, no alcohol. Notifiable disease
- Post exposure prophylaxis with ISG for contacts
- Vaccination:
 - Havrix 1440: 99% immunity after 1 month. One dose im. Booster after 6 – 12 months gives longer-term immunity. Inactivated HAV
 - Especially for travellers, sewage workers, health and childcare workers
 - Can't distinguish natural immunity from vaccine immunity (IgG Anti-HAV in both)



Hepatitis B

Epidemiology

- 350 million with chronic infection, >75% of these Asian
- 30% of chronically infected die prematurely from the disease
- In NZ, approx. 50,000 carriers. Chinese 10%, Maori 5.4%, PI 4.4%, European 0.43%
- Transmission:
 - Body fluids (blood, semen), including transfusion & contaminated needles
 - Mother to baby (vertical transmission): 95% risk of infection – vaccinate at birth and give Anti-HBs – immune globulin
 - Organ transplant
 - Child to child (horizontal transmission). Must get into blood – e.g. grazes, stubbed toes. Very resilient virus. Children are most likely to have asymptomatic seroconversion

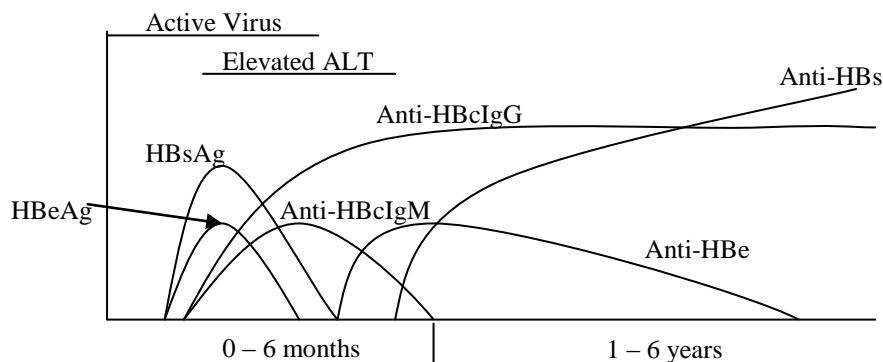
Diagnosis

- ALT elevation to 1000-1500 (usually higher than for Hep C)
- Viral antigens:

	Antigen	Antibody
Surface	HBsAg	Anti-HBs
E (fraction of core)	HBeAg	Anti-HBe
Core	HBcAg (never in blood)	Anti-HBc, IgM Anti-HBc

- Acute Viral Hepatitis due to HBV with recovery:

Jaundice



- Diagnosis from bloods:
 - With HBsAg, HBeAg, and HBV DNA by PCR.
 - Acute HBV: IgM Anti-HBc
 - Carrier: HBsAg
 - Past infection: IgG Anti-HBc
 - Vaccine immunity: IgG Anti-HBs > 10 IU
- Monitoring for carrier state: Test for HBsAg:
 - Monthly for first 6 months or until negative
 - If still positive at 6 months then probably carrier: test 6 monthly till 2 years
 - Annually thereafter
 - Also test ALT
- Carrier infectivity:

	HBsAg	HBeAg	Anti-HBe
High	+	+	-
Intermediate	+	-	-
Low	+	-	+

 - Presence of HBe has a high correlation with the presence of whole hepatitis virions in the blood
- Screening:

	Anti-HBc	HBsAg	Anti-HBs
No infection	-	-	-
Vaccinated	-	-	+
Carrier	+	+	-
Past infection: non infectious	+	-	+
Past infection: low infectivity, silent carrier	+	-	-
- Normal virus called ‘wild type’. Also pre-core mutant HBV virus – doesn’t produce E antigen but will still be HBV-DNA +ive

Progression

- Incubation 45 – 180 days
- Symptoms:
 - Incubation: can be up to 6 months or longer
 - Minority of first episodes are symptomatic
 - If symptoms occur: malaise, anorexia, nausea, jaundice. Coincide with appearance of Anti-HBc antibody in serum
- Acute HBV infection leads to:
 - 10% chronic infection (‘carrier’ is a misnomer) due to ineffective immune response. 90% of infected newborn infants, 25% in young children, and 2 % adults. 25% of ‘carriers’ develop chronic active hepatitis and cirrhosis, and 50% have hepatocellular carcinoma peaking in the 5th decade
 - 65% transient subclinical infection → 100% recovery
 - 25% acute hepatitis → 99% recover, 1% → fulminant hepatitis

- Stages of illness:
 - Immune tolerant stage (mainly babies): no hepatitis even though circulating virus. HBsAg, HbeAg in blood
 - Immune activation → ↑ALT
 - If chronic: called chronic lobular hepatitis (CLH) or chronic active hepatitis (CAH). 6% will clear it per year. Key issue is how much fibrosis has occurred before clearance
 - First stage of clearance: E antigen seroconversion. ↓HBeAg and ↑anti-HBe (was there previously – but used up too rapidly to detect. As HBeAg↓, residual anti-HBe↑)
 - Second stage: S antigen seroconversion

Vaccination

- Most effective means of control: vaccination: Engerix B. 85 – 90% efficacy
- Yeast derived subunit vaccine.
- Number of notifications has dropped from 400 to 100 since introduction in 1988
- Suspension of synthetic HBsAg
- Doses at 0, 1 and 6 months → immune levels of Anti-HBs in 92%.
- Check for seroconversion 2 months later
- Booster every 2 – 3 years if high risk

Treatment

- Lamivudine
 - Purine nucleoside analogue: inhibits DNA polymerase. Potent inhibitor of HBV replication
 - As safe as placebo, no interactions, excreted unchanged
- Each year of treatment:
 - 17% HBe seroconversion (30% if concurrent interferon)
 - 15% get YMDD mutant → ↑ALT and ↑HBV DNA again. But these also seem to seroconvert in time
- Eligibility:
 - If ALT > 2 * normal
 - Pre & post liver transplant
 - HIV and HBV co-infection (plus multi drug therapy for HIV as well)
- Risk of Hepatocellular carcinoma – related to length of time as a carrier

Hepatitis C

- An enveloped ssRNA virus (used to be called non A non B). 6 genotypes identified.
- Damage is caused by immune response – not virus

Presentation

- Incubation to onset of symptoms average 7 weeks (range 3 – 20)
- HCV RNA detectable within 1 – 3 weeks of exposure. Rises rapidly to 10E6 – 10E8 per ml
- Only 1/3 have symptoms.. Clinical illness (if any) lasts 2- 12 weeks
- ALT elevation to 300 – 800
- 50% go on to chronic infection (ie higher than Hep B)
- May present with end stage liver disease (e.g. may present for first time with variceal bleeding)
- Hepatocellular carcinoma found in 1/3, test with ultrasound. ?Evidence that interferon for 6 months ↓risk of HCC

Risk Factors

- NZ prevalence: 0.47%
- Low infectivity: mainly transmitted by blood
- Transfusion
- IV drugs (40-60% of cases)
- Sexual contact (very low risk)
- Maternal transmission to neonate in 5% of maternal infection (ie low risk)

Viral Serology

- Acute HCV: Anti-HCV doesn't appear for 3 months. Can do PCR. Exclude HAV, HBV, EBV, and CMV
- Chronic HCV: Anti-HCV antibody

- Indications for HCV test:
 - Chronic hepatitis (raised ALT over 6 months)
 - History of Non-A, Non-B hepatitis but at least 3 months after acute infection
 - At risk groups: IV users, haemophiliacs
 - Donors: blood and organs
- Indications for HCV RNA test. Test if indeterminate Anti-HCV results, diagnosis in neonates and monitoring of interferon therapy.
- 80% of chronically infected have persisting viraemia

Tests

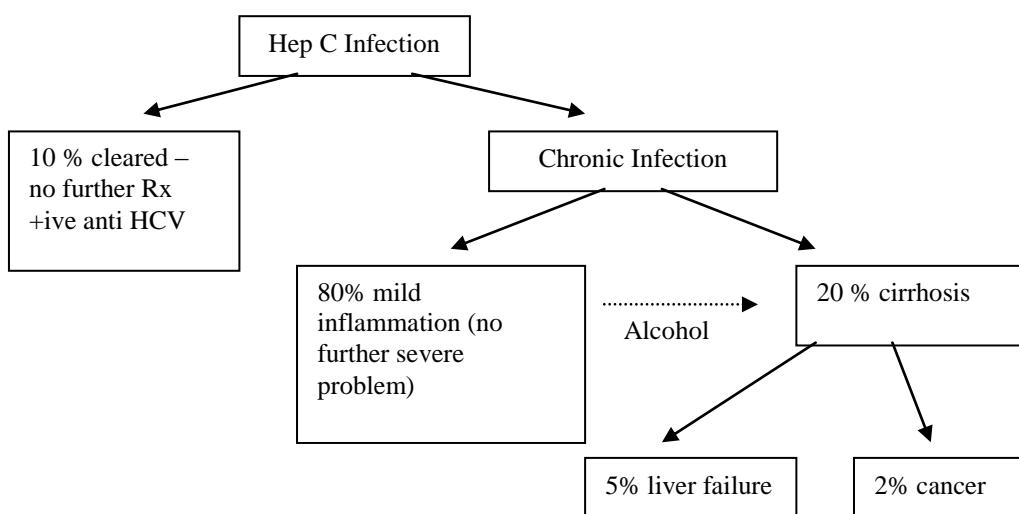
- LFT: bilirubin, Albumin
- FBC: platelets
- APTT/INR
- Anti HCV antibodies
- PCR for HCV RNA
- Ultrasound for size (& to guide biopsy)
- ?Biopsy → degree of fibrosis → prognosis
- Exclude: Hep A, Hep B, Iron studies, ANA

Progression

- If self-limiting HCV RNA undetectable and ALT back to normal in 1 – 3 months
- Wide spectrum: 1/3 persistently normal ALT. Majority fluctuating ALT (⇒ immune system active and causing hepatocyte death). ALT height doesn't correlate with histological severity. Acute – ALT 10 times normal
- Non-hepatic manifestations: arthritis, dry membranes, lichen planus (white plaques in mouth), glomerulonephritis, cryoglobulinaemia, porphyria cutanea tarda (PCT – blisters on skin)

Prognosis

- Contributing to progression:
 - Alcohol → ↑fibrosis
 - HBV
 - Age at infection - younger have longer period of time with infection
 - Mode of acquisition: transfusion worse (?greater viral load)
 - Genotype of virus: effects interferon treatment. Type 1 → severe disease and poor response to interferon



Management

- ↓Alcohol
- Have liver biopsy before commencing drug treatment. Also, intravenous drug users should have drug free urines (otherwise risk of reinfection)
- Need strong motivation/compliance

- Interferon - best for:
 - High ALT
 - Disease < 5 years
 - Non-cirrhotic
 - Not genotype 1
 - Low viral load
 - No history of depression (interferon can cause this)
 - Causes flu like symptoms: ↓appetite, fever, myalgia. Largely resolves after 1-2 weeks. Given it up-regulates the immune system can also cause ↑autoimmune diseases (e.g. thyroid)
 - On its own only 15% are PCR negative 6 months after completing treatment
- Combination interferon/Ribavirin
 - Ribavirin is teratogenic: contraception needs to be VERY reliable
 - Purine nucleoside analogue
 - Stored and transported in red cells. Dose dependent haemolysis ⇒ monitor HB and reticulocytes
 - Only useful in addition to interferon
 - After 3 months, 35% non-responders. 65% complete responders. For genotypes 2 & 3 most of these go on to be sustained responders
- Transplantation:
 - Hep C most common indication
 - Recurrent (usually mild) infection of graft
 - Survival: 65% at 5 years

Other Viral Hepatitis

Hepatitis D

- Defective virus that can only replicate in the presence of HBV infection (requires HBsAg as a viral coat)
- Common in Middle East, Pacific Islands
- Clinical:
 - Acute D on Acute B: in IV drug users. Often severe/fulminating
 - Chronic D on Chronic B: endemic in many parts of the world. Perinatal transmission
- Complications: Chronic hepatitis more common in HBV carriers who are also infected with HDV
- HBV vaccination also protects against HDV

Hepatitis E

- Faecally transmitted: contaminated food and water
- Epidemic in India, China, Russia, parts of Africa
- Higher mortality than HAV, up to 20% in pregnant women
- Test for IgM-specific antibody

Epstein Barr Virus

- 1% of infections present as acute viral hepatitis, with significant elevation of ALT (mild ↑ALT in most cases)
- See Epstein Barr Virus, page 505

Cytomegalovirus (CMV)

- See Infectious diseases chapter

Tumours of the Liver

- Metastases are the most common

Hepatocellular carcinoma

- Epidemiology:
 - 80% of all liver primary cancer
 - Third world: 40% of all cancer, age 20 – 40
 - Western world: age 60+

- Pathogenesis:
 - Hepatitis B: Commonest where carrier state begins in infancy. Viral DNA integrates into the genome
 - Cirrhosis: chronic regenerative activity
 - Fungal toxins: aflatoxin, mycotoxin
- Macroscopic appearance: Either large, unifocal mass, multifocal widely distributed nodules, or infiltrative cancer. Yellow-white masses, occasionally bile stained
- Microscopic appearance:
 - Well differentiated: Trabeculae and acini of malignant cells, large irregular nuclei, bile pigment, cytoplasmic inclusions
 - Anaplastic: giant cell, small cell, spindle cell
 - Fibrolamellar carcinoma (important variant): Single mass with fibrous bands, well-differentiated cells. No cirrhotic background. In kids/young adults. Better prognosis

Cholangiocarcinoma

- Arises in intrahepatic biliary tree
- Associated with parasitic infestation (ie 3rd world)
- Microscopic appearance: well to poorly differentiated adenocarcinoma. Malignant ductules in a dense stroma
- Clinical: ill defined upper abdo pain, malaise, fatigue, enlarged nodular liver, poor prognosis due to late presentation

Rarer Cancers

- Angiosarcoma: malignant tumour of blood vessels. Haemorrhagic appearance in liver. Associated with vinyl chloride (ie plastics manufacture) and arsenic
- Hepatoblastoma: In infants, can be epithelial or mixed, recapitulates foetal liver

Benign Tumours of the Liver

- Bile duct adenoma: “von Meyenberg complex”, 1 cm pale nodules composed of small ducts in fibrous tissue. Incidental finding at surgery
- Liver cell adenoma:
 - Associated with oral contraceptives, pregnancy, anabolic steroids. Rupture can lead to massive haemorrhage (eg in pregnancy).
 - Appearance: soft-yellow bile stained well-circumscribed nodules. Sheets and cords of polygonal cells, lack normal architecture. No features of malignancy (although mildly pleomorphic)
- Other: Cavernous haemangioma, biliary cysts, focal nodular hyperplasia

Other Liver Diseases

- Toxic: drugs, alcohol
- Fatty Liver: obesity, diabetes, drugs, alcohol
- Drugs: e.g. flucloxacillin (and other antibiotics) can cause intrahepatic cholestasis

Haemochromatosis

- Bronzed diabetes: triad of micronodular cirrhosis, diabetes mellitus, and skin pigmentation (iron stimulates ↑ melanin)
- Affects liver, pancreas, heart, gonads. Also causes osteoarthritis and diabetes
- Primary/idiopathic/genetic:
 - Common autosomal recessive, usually males 40 – 60 years. Most common genetic disorder. Homozygotes: 65 – 100% will have iron overload. Heterozygotes have elevated ferritin but no disease
 - Die from hepatocellular carcinoma, cardiac disease, liver failure
 - Iron accumulates in the cytoplasm of liver cells (lots of black dots), also in pancreas, endocrine glands, skin, myocardium, joint linings
 - Macroscopic appearance: micronodular, brown, cirrhotic liver. Atrophy and fibrosis of pancreas. Enlarged heart. Brown/grey skin
 - Microscopic appearance: Initially golden brown periportal ferritin deposits in hepatocytes. Later Kupffer cells become loaded. Non-inflammatory cirrhosis. Pearl stain: stains iron blue
 - Monitoring:
 - If transferrin > 45% or serum ferritin > 300 ng/ml then liver biopsy if > 39 years
 - Hepatic Iron Index = hepatic iron concentration/age. Normal < 1.9 mmol/gm/yr

- If cirrhosis for > 10 years then screen for hepatocellular carcinoma every 6 or 12 months. If picked up clinically then too late
- Screen for α -feta Protein (tumour marker), or inject lipiodol into hepatic artery → preferentially taken up by HCC → hypodense on CT
- Treatment of HCC: resection or liver transplantation. Chemo ineffective
- Treatment of haemochromatosis: if regular venesection before organ damage then normal life expectancy. Regular initial venesection to $\downarrow\downarrow$ iron load, then venesection every 3 – 6 months
- Secondary:
 - Ineffective erythropoiesis (eg thalassaemia, liver disease, high iron intake)
 - Iron first in Kupffer cells, later in hepatocytes
 - Cirrhosis unusual

Diseases of Intrahepatic Bile Ducts

- Ascending Cholangitis
 - Suppurative inflammation within the bile ducts with bile stasis
 - Caused by obstruction, treated with drainage
 - Common organisms are enteric: E Coli, Klebsiella, Enterobacilli
- Primary Sclerosing Cholangitis
 - Autoimmune destruction of intra *and extra* hepatic bile ducts
 - In young males, associated with ulcerative colitis and HLA types
 - Cirrhosis and liver failure within 5 years
 - Microscopic appearance: onion skin fibrosis around intrahepatic ducts
- Primary Biliary Cirrhosis:
 - Autoimmune destruction of intrahepatic ducts
 - F:M = 9:1, average age = 50
 - Antimitochondrial antibodies typical
 - Focal inflammatory destruction of bile ducts, no primary inflammation in stroma → ducts reduced in number → green bile plugs in canaliculi → bile infarct and portal-portal fibrosis → cholestasis and cirrhosis
- Secondary biliary cirrhosis: scarring following obstruction and ascending cholangitis
- Disappearing bile ducts: Autoimmune, Graft vs. Host, Post transplant – all due to lymphocytic destruction of biliary epithelium

Vascular Disease of the Liver

- Post hepatic disease:
 - Right sided heart failure:
 - Enlarged, tense, tender liver
 - Marked centrilobular congestion and haemorrhagic necrosis: ‘nutmeg liver’ – lacy pattern with dark and light areas
 - Cardiac Sclerosis:
 - Less common complication of heart failure
 - A peri-venular fibrosing reaction following long-standing congestion
 - Rarely causes ↑portal pressure
 - Hepatic Vein Thrombosis (Budd Chiari Syndrome)
 - Hepatic congestion from obstruction to blood flow due to occlusion of hepatic veins or IVC
 - Associated with anything causing hypercoagulability: polycythaemia vera, pregnancy, oral contraceptives, hepatocellular carcinoma
 - Appearance: swollen, red liver, congestion, veins containing thrombi
- Intrahepatic Disease: Hepatic veno-occlusive disease. Subendothelial sclerosis of veins. Lumen of central vein occluded + collagen deposition in Space of Disse
- Pre-hepatic disease: Portal vein obstruction due to cancer, peritoneal sepsis, pancreatitis, surgery, cirrhosis

Gilbert's Syndrome

- Normal variant in ?7% of the population
- Raised indirect bilirubin due to ‘defective’ uptake and conjugation of bilirubin by liver
- Exacerbated by low fat/low calorie diet (e.g. when gastroenteritis). Use this to test: fast and see if it increases. Also worse when ill due to other causes (may present as a red hearing)
- Bilirubin rarely > 100 micromol/L

- Is totally benign

Neonatal Liver Disease

- Extrahepatic Biliary Atresia: destructive inflammation of bile ducts → cirrhosis
- Neonatal Hepatitis: non-specific idiopathic response to neonatal hepatic insult (eg virus). Giant cell transformation of hepatocytes, chronic inflammation around portal tracts, focal necrosis and lobular disarray

Wilson's Disease

- Rare autosomal recessive: accumulation of dietary copper in liver, brain, eye
- Leads to non-inflammatory cirrhosis
- Can look like alcoholic liver disease due to Mallory hyaline and bile plugging

Alpha-1 Antitrypsin Deficiency

- Autosomal co-dominant.
- → Ineffective protease inhibitor enzymes
- Genetics:
 - Only liver disease if < 10% normal function (ie ZZ allele).
 - Z is bad, M is normal, S is mildly impaired. Only 10% of ZZ get chronic liver disease.
 - 7 – 10% of the population have a variant associated with mild/moderate deficiency
- Abnormal alpha-1AT accumulates in cells as cytoplasmic globules → cell death → fibrosis
- Clinical: neonatal hepatitis, can present as macronodular in adult. Suspect in premature emphysema

End Stage Liver Disease

Hepatic Failure

- Conjugated jaundice
- Fatigue, muscle wasting, bruising
- ↓Platelet count (reliable early indicator of cirrhosis)
- ↓Synthesis: notably of albumin
- Fluid retention, ascites, spontaneous bacterial peritonitis
- Coagulopathy: ↓synthesis of 2, 5, 7, 9, 10
- Hyperammonaemia → metabolic encephalopathy
- Gynaecomastia (steroid hormones not metabolised)
- Hepatocellular carcinoma
- Hepato-renal Syndrome:
 - Renal failure in patients with liver failure → ↑urea and creatinine
 - Blood is hyperosmolar but urine sodium is low
 - Pathogenesis unknown: possibly vasoconstriction
- Hepatic Encephalopathy:
 - Metabolic derangement of the brain: only mild morphologic changes (eg oedema)
 - Flapping tremour
 - Grade 1 – altered mood, confusion, 2 – drowsy, disorientation, ataxia, 3 – marked confusion, sleepy, obey simple commands, 4 - coma
- Which lead to liver failure or transplantation

Portal Hypertension

- Diagnosed clinically: if cirrhosis, ascites and varices assume portal hypertension. Can confirm with Doppler ultrasound
- Causes:
 - Post-hepatic: vascular outflow obstruction (Budd Chari Syndrome)
 - Intrahepatic: cirrhosis
 - Prehepatic: portal vein occlusions
- Consequences:
 - Ascites: ↓albumin synthesis, ↑portal pressure, ↑hepatic lymph formation and renal retention of sodium and water
 - Portosystemic shunts: oesophageal varices, haemorrhoids and abdominal wall
 - Splenomegaly and portal congestive gastropathy

- Treatment of varices:
 - Complicated by hypo-coagulopathy secondary to liver failure (do INR and APPT)
 - Band oesophageal varices lower down: collapses them further up. Varices are asymptomatic until eroded by acid or increased pressure from vomiting
 - Emergency therapy for bleeding varices:
 - Octreotide infusion (somatostatin analogue but longer T $\frac{1}{2}$) → reduce portal pressure
 - Balloon tamponade
 - Resuscitation
 - Then emergency endoscopy with sclerotherapy (takes several iterations) or banding, or TIPS/surgery (portal/caval shunt)
 - Maintenance treatment:
 - Sucralfate (an Al carbohydrate): 1 gm 1 hr ac QID - surface protective effect to stop ulcers over sclerosed varices
 - Beta blocker: propranolol, nadolol → ↓CO due to ↓HR

Nutrition

- Malnutrition is common in chronic liver disease due to ↓absorption and ↓synthesis
- Give ↑fat and ↓CHO to combat hyperglycaemia resulting from insulin resistance
- If encephalopathy, then low protein diet, antibiotics to decrease bacterial ammonia production and lactulose (↓transit time & metabolised by bacteria → ↑H⁺ which converts NH₃ to less absorbable NH₄)

Gallbladder and Bile Ducts

- Cholecystitis = inflamed gallbladder (eg due to stone impacted in gallbladder or cystic duct). Acute or chronic
- Cholangitis = bile duct infection: RUQ pain, jaundice & rigors
- Choledocholithiasis = gallstones in common bile duct
- Cholecystolithiasis = gallstones in gallbladder (??)
- Cholecystectomy = gall bladder out

Cholelithiasis

- = Gall stones.
- Cholesterol stones:
 - 85% of stones
 - Incidence: Northern European ancestry, ↑age, female, obesity
 - Caused by supersaturation of the bile with cholesterol → precipitation around bits of junk (eg epithelium)
 - Appearance: either pure pale yellow and radiolucent, or mixed grey ‘gravel’ – more dangerous as can squeeze through cystic duct
- Pigment stones:
 - 15% of stones
 - Incidence: Asian, haemolysis, alcoholic cirrhosis, biliary infection, ↑age
 - Excess unconjugated bilirubin
 - Appearance: small, jet black and ovoid

Cholecystitis

Biliary Colic

- Symptoms:
 - Gives a *colicky* pain – waves of intense pain every 10 – 20 minutes with little pain in between. Patient is restless – can’t get comfortable in any position (as opposed to cholecystitis below)
 - May be mild tenderness on examination
- Pathogenesis:
 - Impaction of stone in the cystic duct
 - No inflammation of the gall bladder (yet)
- Investigations:
 - Plain xray (mainly to exclude other causes of an acute abdomen – eg obstruction, perforation, etc)
 - Diagnosis by US – looking for a thickened wall on the gall bladder and filling defects in the ducts

- CT the best modality for looking for stones
- Management:
 - IV fluids (may not have been drinking, may need to be nil-by-mouth if they go to surgery)
 - Bloods: FBC, U&Es, LFTs, Amylase, Clotting factors, Group & Hold, ESR/CRP
 - Urine: UTI/pregnancy
 - Pain relief + antiemetics
 - Antibiotics
 - Antispasmodics (eg Buscopan) for colic

Acute Cholecystitis

- Most dangerous common complication of cholelithiasis
- Clinical presentation: acute abdomen. Symptoms may be obscured by the predisposing condition
- 90% caused by impaction of stone in the neck: calculus acute cholecystitis. If no stones then acalculous cholecystitis (usually vasculitis)
- ↑Inflammation due to ↑pressure, chemical irritation, and secondary infection
- Macroscopic appearance: enlarged (bigger than chronic), tense, covered by fibrin, contains turbid bile or puss. Wall is thick and oedematous and the mucosa is red or green-black (gangrenous cholecystitis, due to ↓blood flow secondary to ↑pressure)
- Microscopic appearance: Acute inflammation, congestion, abscess, necrosis
- Symptoms:
 - 70% stones are asymptomatic. If symptomatic there is a 30% 5 year risk of complications requiring surgery
 - Uncomplicated: severe *constant* epigastric/RUQ pain, lasting several hours, radiating to back, maybe nausea/vomiting. It hurts to move or breath so patient lies still. Local peritonitis (very tender). If impacted then inflammatory component (fever, ↑WBCs)
 - Complicated:
 - Fever, abdominal pain, nausea, vomiting: indicating acute cholecystitis
 - Fever, pain, jaundice: acute cholangitis
 - Abdominal and back pain, collapse, vomiting, hypotension: acute pancreatitis
- Investigations
 - Murphy's sign: Lay 2 fingers on RUQ. Patient inspiration → pain. No pain on LUQ
 - Gallstones often incidental finding on ultrasound or x-ray (if calcified – only 10% radio-opaque)
 - Ultrasound picks up 98% of gallbladder stones but only 50% of common bile duct stones. More can be inferred from a dilated duct (> 6 mm)
 - Serum Amylase: if > 1000 IU/L ⇒ acute pancreatitis
 - ALP & bilirubin
 - WBC count → cholecystitis
 - Antimitochondrial antibody tests → exclude primary biliary cirrhosis
- Differential
 - Obstructive Jaundice: pancreatic neoplasm, cholestatic hepatitis
 - Biliary colic: pancreatitis, oesophagitis, peptic ulcer, IBS
 - Ascending Cholangitis
- Treatment
 - If acute, nil by mouth, pain relief, IV antibiotics (e.g. cefuroxime)
 - Usually settle with conservative treatment (wait 2 days and see). Then schedule for elective cholecystectomy 6 week later (once inflammation settled down)
 - Surgical Options:
 - Lithotripsy
 - Laparoscopic cholecystectomy
 - Percutaneous, transhepatic gallbladder canulation (PTC)
 - Long term:
 - No relationship with high-cholesterol diet. Avoid obesity
 - Drugs: bile acid treatment – dissolve small cholesterol stones

Chronic Cholecystitis

- ?Aetiology: no infective or inflammatory agents
- Macroscopic appearance: normal to enlarged gallbladder with stones and a fibrous thickened wall

- Microscopic appearance: chronic inflammation, fibrosis and muscular hypertrophy. Rokitansky-Aschoff sinuses: herniations through submucosa. Lipid laden macrophages extend into the lamina propria
- Symptoms: heartburn, belching, intolerance of fatty foods, discomfort. Can be found in people without gallstones ⇒ symptoms not specific

Ascending Cholangitis

- Signs of Acute Cholecystitis plus sweats and rigours
- Infection of the biliary tract
- Often accompanies obstruction due to gall stones
- Also following ERCP (probe introduces gut bacteria into the ducts which are normally sterile)
- Can be rapidly fatal – have low threshold for treatment
- Rare differential Mirizzi Syndrome: no stone in the common duct but its compressed by adjacent inflamed gallbladder

Mucocoele of the Gallbladder

- Cystic duct becomes obstructed. Trapped bile is absorbed and gallbladder fills with mucus

Tumours

- Benign tumours:
 - Adenomas and papillomas: project into the lumen. Benign overgrowths of epithelium
 - Adenomyoma: nodule at the gallbladder tip composed of smooth muscle around benign ductules
- Malignant:
 - Carcinoma of the gallbladder:
 - Uncommon: 0.5% of cholelithiasis patients
 - Associated with gallstones and inflammation
 - Presentation: insidious until late. Abdo pain, jaundice, anorexia, weight loss, nausea. 1% 5-year survival
 - Macroscopic appearance: at fundus and neck. Either infiltrating or fungating type. At discovery usually involve liver, bile ducts and portal nodes
 - Microscopic appearance: 95% adenocarcinoma (can be poorly differentiated), 5% squamous cell carcinoma (from squamous metaplasia)
 - Carcinoma of the bile ducts and ampulla:
 - Uncommon, associated with chronic inflammation, parasites, ulcerative colitis
 - Presentation: obstructive jaundice, pale stools, nausea, ↑LFTs. Differentiate from obstruction due to stones. Poor prognosis
 - Macroscopic appearance: papillary fungating mass + intraductal nodules + diffuse infiltration → obstruction. Periampullary tumours have better prognosis
 - Microscopic appearance: adenocarcinoma, occasionally squamous cell

Pancreas

Acute Pancreatitis

- = Inflammation in pancreas and peripancreatic tissues (sometimes with haemorrhage and necrosis)

Causes

- 90% caused by either (grog or gravel):
 - Gallstones blocking the ampulla (60%)
 - Alcoholic (more chronic than acute) (30%). Pathogenesis unclear - ?duct obstruction
- Also: trauma, ERCP, drugs
- Types:
 - Interstitial or oedematous pancreatitis: mild, self-limiting
 - Acute haemorrhagic (necrotising) pancreatitis: severe

Pathogenesis

- Activation of pancreatic enzymes → cellular injury, release of enzymes and cytokines → ischaemia. Secondary bacterial infection possible. May also follow ERCP – catalysts from duodenum activate pancreatic enzymes while still in the pancreatic duct
- Macroscopic appearance:

- Variegated: blue-black haemorrhage, yellow-white fat necrosis
- Peritoneal ‘Chicken-Broth Ascites’: layer of clear fat floating on turbid liquid – lipase has digested abdominal fat
- With resolution: fibrosis, calcification, pseudocysts
- Microscopic appearance: If mild, periductal inflammation. Proteolytic destruction of the pancreatic substance. Necrosis of blood vessels → haemorrhage

Presentation

- Upper abdominal *constant* (ie inflammatory) pain + lumbar back pain
- Nausea, vomiting
- Peritoneal irritation, ileus
- Jaundice, especially in gallstone induced
- Tachycardia
- Signs (due to haemorrhagic fluid in the extra peritoneal space):
 - Cullen’s Sign: Discolouration around the umbilicus
 - Greg-Turner’s Sign: Discolouration around the flanks
- If severe:
 - Shock: enzymes into blood, acute peritonitis, massive inflammation
 - Respiratory failure, circulatory failure
- Complications: shock, ARDS, acute renal failure, abscess, duodenal obstruction

Investigations

- ↑ Serum or urine amylase. Height of amylase does not correlate with severity. Other conditions may cause raised amylase. ↑ Lipase
- Also possibly ↑ glucose, ↑ WBCs, ↑ creatinine, ↓ calcium, ↑ faecal elastase
- CXR to exclude gastrointestinal perforation (air under diaphragm)
- Ultrasound/ERCP, ALT and bilirubin to check for stones
- CT to determine extent of inflammation/necrosis. Use contrast – necrotic tissue doesn’t light up as it’s not perfused
- Also FNA

Differential

- Abdominal catastrophe: perforation, ectopic pregnancy, infarction, ruptured aneurysm, obstruction, appendicitis
- MI
- Acute cholecystitis

Progression

- Most fully recover in 4 – 6 days with IV fluids, O₂, analgesia
- If severe, up to 50% mortality. Treat for renal, cardiac and respiratory failure. Surgery for infected necrosis
- Treat cause: e.g. ERCP + sphincterotomy, later cholecystectomy, alcohol abstinence, etc
- Supportive treatment: IV fluids, pain relief, inotropic support if ↓BP or renal hypoperfusion despite fluids

Chronic Pancreatitis

- = Replacement of pancreatic tissue by fibrosis, often with calcification, sometimes with duct dilation and stones
- May result in chronic pain, relapsing acute pancreatitis, exocrine or endocrine deficiency

Causes:

- Alcohol (60 – 80%) → duct obstruction by protein rich secretions
- Obstruction (10%)
- Idiopathic (10%)
- Genetic factors
- Hypercalcaemia and Hyperlipidaemia
- Congenital anomalies of duct
- Following acute pancreatitis of any cause

Symptoms

- Abdominal pain, weight loss, diarrhoea/steatorrhoea, diabetes mellitus (late complication – islet cells are the last to fail), acute pancreatitis

Investigations

- As for acute, plus check chronic differentials (e.g. ulcer, GORD)
- Blood glucose, GTT

Pathology

- Chronic calcifying pancreatitis:
 - In alcoholics
 - Macroscopic appearance: throughout lobules of pancreas, hardened foci of calcification
 - Microscopic appearance: atrophy of acini, fibrosis, chronic inflammation. Dilated ducts and atrophic epithelium
- Obstructive pancreatitis
 - Due to cholelithiasis
 - Affects periductal regions, mainly head of the pancreas
 - Ductal epithelium better preserved

Treatment:

- Exocrine/endocrine replacement
- Analgesia
- Surgery: duct dilation, resection of diseased portion

Pancreatic Tumours

Symptoms

- Weight loss, anorexia, lethargy
- Pain
- Jaundice (70%)
- Pruritis (itching)
- Diabetes mellitus

Investigations

- FBC: anaemia, sepsis
- LFT: to confirm obstructive jaundice
- Ultrasound
- ERCP or CT

Differential

- Obstructive jaundice
- Hepatic jaundice
- Cachexia: gastric, colorectal or ovarian cancer
- Other pancreatic disease

Types

- Pseudocysts (don't have epithelial lining so not a true cyst – not neoplastic):
 - Congenital (rare) or acquired
 - Solitary cyst 5 – 10 cm diameter, contains serous, turbid fluid
 - Associated with pancreatitis
- Benign tumours: rare. Serous cystadenoma (elderly women), solid cystic tumour (young women)
- Carcinoma of the pancreas
 - Epidemiology:
 - 5% of cancer deaths
 - Usually fatal, 90% die within one year, 5 year survival 1 – 2%
 - Associated with smoking, fatty diet, chemical carcinogens
 - M > F, B > W, 60+
 - Presentation:
 - Often perineural invasion (travels along nerves) → difficult pain

- Affecting head: obstructive jaundice
- Affecting tail: weight loss, liver metastases
- Macroscopic appearance: 60% head (most pancreatic tissue is there). Grey-white tumour with infiltrative margins. Extends to duodenum, liver, nodes, etc
- Microscopic appearance: 90% adenocarcinoma, 10% adenosquamous. Other rare types
- Treatment: palliative. Stenting or ERCP for duct compression
- If resection possible:
 - For body/tail: distal pancreatectomy – usually need to remove spleen as well
 - For head: pancreaticoduodenectomy (Whipple operation)
- Other tumours: benign or malignant endocrine tumours (insulinoma, gastrinoma)

Renal and Genitourinary

- References: Renal Medicine handout, General Medicine Run, and Prof Delahunt's pathology handout
- See also Renal Disease in Children, page 632

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History

- Exposure to nephrotoxic medication (i.e. pre-renal or intrinsic renal failure)
- Risks of renal-artery atherosclerotic disease
- Volume depletion \Rightarrow pre-renal
- Rash = allergic interstitial nephritis
- Bone pain in elderly \Rightarrow multiple myeloma \rightarrow acute renal failure

Renal Physiology

- Function of kidneys:
 - Maintenance of fluid and electrolyte balance
 - Excretion of metabolic wastes
 - Excretion of acid
 - Endocrine (calcitriol, erythropoietin)
- Allows regulation of a daily intake of:
 - Water: 1 – 20 litres
 - Sodium: 5 – 500 mmol
 - Potassium: 20 – 200 mmol
 - Protein: 30 – 150 g
- Fluid dynamics:
 - Kidney's receive 20 – 25% of cardiac output
 - GFR maintained by autoregulation but dependent on glomerular pressure and renal blood flow
 - Normal urination: 1 ml/kg/hr (down to 0.5 ml/kg/hr OK)
 - Urine output of 1 – 2 litres/day
- Hormones:
 - Intra-renal:
 - Renin-angiotensin system: \downarrow Na, hypotension \rightarrow \uparrow renin \rightarrow \uparrow angiotensin II \rightarrow vasoconstriction, \uparrow aldosterone and thirst
 - Prostaglandins: vasodilating, control glomerular blood flow, natriuretic and diuretic
 - Extra-renal:
 - Aldosterone: stimulated by Angiotensin II and \uparrow K \rightarrow Na reabsorption
 - ADH: controlled by both volume and osmotic stimuli \rightarrow \uparrow water resorption providing sufficient medullary concentration gradient
 - Atrial and brain natriuretic proteins (ANP/BNP): volume overload \rightarrow natriuretic and diuretic
- For hypo/hypernatraemia, potassium and acid-base balance, see Electrolytes, page 107

Assessment of Renal Function

Urinalysis

- **Dipstick:**
 - Blood: indicates bleeding in the urinary tract or free haemoglobin or myoglobin
 - Proteinuria: sensitive to protein – but use 24 hour urine to quantify, or spot check with protein:Cr ratio in morning urine. Urine protein is normally albumin. Hyaline and granular casts and Bense Jones Proteins **don't** test +ive for protein
 - Glucose: diabetes, pregnancy, sepsis, tubular damage or low renal threshold
 - Nitrates \Rightarrow UTI
- **Microscopy:**
 - Blood: should be less than $8 * 10^6$ cells per litre
 - Normal morphology suggests bleeding from the lower urinary tract: calculi, infection, neoplasia
 - Dysmorphic cells suggests glomerular bleeding: glomerulonephritis and vasculitis (including endocarditis). Microhaematuria can be either nephrotic or nephritic. Macro haematuria is normally nephritic
 - WBCs indicate infection, less commonly renal tuberculosis, renal stones and papillary necrosis
 - Eosinophils \Rightarrow interstitial nephritis
 - Casts:

- Hyaline casts: just protein, no cellular elements and may be normal (especially concentrated urine)
- Granular casts: Degenerative cellular material – usually tubular cells \Rightarrow pathology
- Red cell casts: glomerular bleeding \rightarrow usually active GN
- White cell casts: pyelonephritis, interstitial nephritis or glomerulonephritis

Glomerular Filtration Rate (GFR)

- Marker of renal excretory function
- Determined by intra-glomerular pressure, which in turn is determined by the difference in vascular tone between afferent and efferent arterioles. Maintained by autoregulation except when blood pressure is very high or very low
- Creatinine:
 - Filtered at the glomerulus and not reabsorbed, but a small amount is excreted from the tubules (ie GFR less reliable at small urine flows)
 - Affected by muscle mass, protein intake and age \rightarrow poor indicator of renal function. Serial measurements helpful
 - Normal Creatinine < 0.110 mmol/L
- Use Cockcroft-Gault formula:

$$GFR(\text{mL/sec}) = \frac{(140 - \text{age}) * \text{lean body weight(kg)} * 0.85(\text{female})}{50 * \text{serum creatinine(micromil / L)}}$$

- Normal is > 1.5 ml/sec (> 90 ml/min)
- Use total body weight but recognise it overestimates if obese
- Or collect 24 hour urine and compare to plasma concentration with UV/P
- Can measure with radionuclides

Other

- Do volume assessment: lying and standing BP, JVP, change in weight, etc
- Tubular Function: test concentrating ability with fluid deprivation and ADH administration
- Urinary Acidification: give ammonium chloride and then measure urinary pH
- Also consider blood tests: Ca, PO₄, FBC, complement, autoantibodies, etc

Renal Imaging

- Plain X-ray: shows radio-opaque renal stones (90% are) not uric acid stones (eg Gout). Methodology:
 - Gas:
 - Renal colic/pancreatitis \rightarrow focal ileus
 - Emphysematous pyelonephritis \rightarrow gas in kidney
 - Emphysematous cystitis \rightarrow gas in bladder
 - Stripes:
 - Find the psoas muscle and move out parallel to this to find the kidneys
 - Assess size: length of kidney = length of 3 vertebrae + disc spaces. Up to 2 cm variation in size between kidney's OK
 - Stones: check down ureters: down psoas, anterior to sacro-iliac junction, around pelvis, into bladder
 - Bones: renal osteodystrophy, etc
- Intravenous Urogram (Plain film + contrast) = IVU = IVP (Intravenous pyelogram)
 - Gives anatomical and functional information
 - Shows renal contours, presence of scarring, reflux nephropathy, obstruction
 - Depends on renal uptake of the contrast. Little use if significant renal impairment (eg CR > 200)
 - Interpretation:
 - Nephrogram phase (1 minute post injection): renal contour, position, equal in intensity?
 - Pyelogram phase (5 minutes): see major and minor calices and bladder
 - Post micturition phase: look for normal voiding
- Antegrade and retrograde pyelography: direct injection of contrast into the renal pelvis or the ureter
- Micturating Cystourethrogram: Fill bladder with contrast and image following micturition. For assessment of vesico-ureteric reflux in children
- Ultrasound:
 - For renal size and contour

- Shows hydronephrosis – but may not show the site of obstruction. Reasonable view of renal masses and cysts
- Scarring: asymmetric indentation of renal outline. If young → ?reflux. If older → ?ischaemia
- CT: for complex cysts, masses, renal colic and *stones*.
 - Modality of choice for stones. 5 mm slices:
 - ↑Sensitivity
 - No contrast risk (mortality 1 in 40,000)
 - Can sort out differentials of colic (eg appendicitis) on CT that you won't see on IVP
 - Stone filling the whole of the renal calicies = staghorn calyx (in recurrent infection and alkaline urine)
- Nuclear medicine studies:
 - Renogram for assessing function of each kidney, avoids nephrotoxic contrasts. Eg Technetium labelled DTPA and Mag3. Especially good for renal artery stenosis and obstruction
 - DMSA: highlights proximal tubules. Good for showing renal scarring, eg reflux nephropathy
- Arteriography: Renal artery stenosis

Renal Biopsy

- Under local
- Indications: acute renal failure, nephrotic syndrome, heavy proteinuria or haematuria
- Only if histology will influence management
- Major contraindication: bleeding tendency (check FBC and clotting first)
- Complications: bleeding and development of a perirenal haematoma (eg in amyloid disease when rigid arterioles won't contract following bleeding)
- Risk of serious complications < 1% (fistula, haematoma, infection, surgery, etc)

Presentation of Kidney Disease

- This section outlines how kidney diseases present. A variety of kidney diseases present symptomatically in a variety of different ways. The major underlying diseases are described in the following section of Kidney Diseases, page 210
- Other presentations of kidney disease:
 - Hypertension: common symptom of chronic renal failure of any cause
 - See Renal Osteodystrophy in Increased Bone Resorption, page 263
 - See Urinary Tract Infections, page 219

Nephritic Syndrome

- ~ Proliferative glomerulonephritis
- Presentation:
 - Urinary sediment: haematuria, granular and cellular casts
 - Varying degrees of proteinuria
 - Oliguria → fluid retention and oedema
 - Renal impairment → ↑Cr, electrolyte disturbance
 - Hypertension
 - Headache
- Histology: Large glomeruli (diffuse changes of predominantly mesangial cells), polymorphs and black deposits on epithelial side of BM, can occasionally lead to crescents (ie lots of cell proliferation compared with Nephrotic Syndrome ⇒ rapidly progressive glomerulonephritis)
- Possible causes:
 - Post-infectious GN
 - Rapidly progressive GN
 - Mesangio-capillary GN
 - Maybe IgA GN

Nephrotic Syndrome

- ~ Non-proliferative glomerulonephritis
- Presentation:
 - Marked proteinuria (may make urine frothy) > 3 g/day
 - Hypoalbuminaemia → oedema: generalised, insidious onset, may be peri-orbital in the morning, legs in the afternoon. If gross then ascites and pleural effusion

- Hypercholesterolaemia
- Renal function is preserved. But may retain Na and H₂O. May ↑ plasma volume
- If polyuria then ⇒ tubular and interstitial damage as well
- Pathogenesis: common end point of a variety of disease processes that alter the permeability of the basement membrane
- Possible causes (first 3 reasonably common in adults, Membranous is perhaps the most common):
 - Minimal change GN
 - Membranous GN
 - Focal Segmental GN
 - Maybe IgA and mesangiocapillary
 - (Also diabetes, amyloidosis (eg multiple myeloma), drugs)
- Management:
 - Minimal change: very responsive to steroids. The rest need something stronger (eg cyclophosphamide) and commonly → renal failure over time
 - Fluid restrict
 - Monitor and treat BP
 - Salt restricted, high protein diet
 - Oral diuretics + K (beware hypovolaemia → pre-renal failure)
- Complications: loose Antithrombin 3 protein as well as albumin → renal vein (and other) thrombosis.
?Prophylactic anticoagulation

Acute Renal Failure

- =Abrupt reduction in glomerular filtration rate → ↑plasma urea & creatinine and (usually) ↓urine volume (oliguria < 400 ml/day,uria < 100 ml/day). If ↑↑urea but only ↑Cr then ?dehydration or catabolic state
- Assess severity using Cockcroft-Gault equation (see page 203). Normal clearance >= ~ 100 ml/min
- Due to acute damage to any part of the kidney or renal tract. Usually Acute Tubular Necrosis but always consider differentials

Pre-renal Acute Renal Failure

- =↓ in glomerular perfusion in absence of structural kidney damage
- Kidney usually autoregulates – but can't cope with extremes
- Can't interpret results if patient has had recent diuretics
- If prolonged → ischaemic damage → loss of medullary gradient and reabsorbing capacity → dilute urine
- Causes:
 - Volume depletion: Usually GI loss, but also renal loss, burns, haemorrhage
 - Cardiac failure → ↓renal perfusion
 - Systemic vasodilation: sepsis or antihypertensives
 - Also:
 - Reno-vascular disease: renal artery stenosis
 - Vasoconstriction in kidneys, e.g. due to NSAIDs (→ ↓vasodilating PGs), ACE inhibitors (→ ↓efferent arteriolar tone → ↓intraglomerular pressure)
- Intense reabsorption of salt and water leads to:
 - Low volume of urine, high osmolality (> plasma), but low urine Na (usually < 20 mmol/l)
 - ↑Urine to plasma ratio of creatinine and urea
 - Urea is re-absorbed preferentially to creatinine at low urine flows ⇒ plasma urea to creatinine is increased
 - Hyaline casts: aggregations of urine protein if low urine flow
- Kidneys try to compensate by:
 - Vasodilating afferent arterioles (via ↑PGs)
 - Activation of renin-angiotensin → ↑BP and vasoconstricts efferent arterioles
- Management:
 - Rapid fluid resuscitation
 - Correct underlying disorder (eg inotropes)
 - Monitor intravascular volume and watch for ATN

Intrinsic Acute Renal Failure

- Possible presentations:
 - Oliguria (rather thanuria)
 - Nephritic syndrome: haematuria, hypertension, oliguria +/- oedema
 - Proteinuria: excludes pre and post-renal
 - Hypertension: intrinsic renal disease → ↑BP, pre-renal → ↓BP
 - Systemic features of disorders causing intrinsic failure (eg fever, arthralgia, skin rash, vasculitis etc)
- Due to:
 - Acute Tubular Necrosis (most common cause): See page 211
 - Acute Interstitial Nephritis: See page 211
 - RPGN: Urine chemistry midway between pre-renal acute renal failure and acute tubular necrosis - ↑urine to plasma ratios for osmolality and creatinine, and Na between 20 – 40 mmol/L. See page 212
 - Nephrotoxins
 - Other tubular diseases (eg myeloma)
- Investigations:
 - Urinalysis: cells, casts, protein
 - US: ↑echogenicity
 - Renal biopsy
 - Also blood tests to exclude specific causes: ANA, ANCA, Complement, CK, etc

Post-renal Acute Renal Failure

- Presentation:
 - Completeuria: most pre-renal and intra-renal failure is oliguric. But partial obstruction may give moderate tubular dysfunction → osmotic diuresis → polyuria
 - Normal urinalysis: no proteinuria or casts, any blood (eg from stones, cancer) will be normal not dysmorphic
 - Specific diseases pre-dispose: eg diabetes and analgesic use → papillary necrosis → bits fall off and cause obstruction. See Acute Papillary Necrosis, page 211
- Due to obstruction:
 - Usually in urethra: bladder stones or tumours. Prostate usually chronic
 - If at ureteric level must be bilateral to lead to severe kidney failure or obstruction on one side and a poor functioning kidney on the other
 - Extrinsic obstruction due to eg retroperitoneal fibrosis following radiotherapy, etc
- → ↑tubular pressure → ↓glomerula filtration
- Usually obvious from history, confirm with:
 - Ultrasound of kidneys for hydronephrosis
 - CT to determine the level of the blockage
 - IVU only if the kidney is functioning (ie Cr < 200)

Investigations in Acute Renal Failure

	Pre-renal	ATN	RPGN	AIN
Urine Osmolality	>500	<350	300-400	300-400
Urine Na	<20	>40	20-40	20-40
Urine/Plasma urea	>10	<10	Intermediate	Intermediate
Urine/Plasma creatinine	>40	<20	Intermediate	Intermediate
Fractional excretion of Na	<1	>3	<1	>1
Urine Sediment				
RBC	Occasional	+	+++	Occasional
WBC	Occasional	Occasional	++	+++
Granular casts	Occasional	++	++	+
Epithelial casts		+++	++	
RBC casts			+++	
WBC casts				Occasional

- Fractional excretion of Na =
$$\frac{\text{Urine Na} * \text{Plasma Cr} * 100}{\text{Plasma Na} * \text{Urine Cr}}$$

- Renal biopsy is rarely needed to differentiate causes of renal failure, mainly in RPGN

Management

- Treat cause
- Resuscitate if hypovolaemia
- Monitor for ↑K
- Treat pulmonary oedema, ?dialysis
- Monitor fluid balance carefully
- Avoid nephrotoxic drugs

Chronic Renal Failure

- = Reduction in renal function for > 6 months
- Causes in NZ in 1997:

Diabetes Mellitus	44% (and growing)
Glomerulonephritis	20%
Hypertension	13%
Polycystic Kidney Disease	6%
Reflux Nephropathy	3%
Analgesic Nephropathy	< 1%
Miscellaneous	7%
Uncertain diagnosis	7%

- Miscellaneous causes include: stone disease, interstitial nephritis, amyloidosis, myeloma, lithium toxicity, obstructive uropathy, renal cell carcinoma, post-partum failure
- Symptoms:
 - Earlier: nausea, anorexia, lethargy, itch, nocturia, impotence
 - Later: oedema, SOB, chest pain (from pericarditis), vomiting, confusion, fits
- See also:
 - Adult Polycystic Kidney, page 216
 - Wegner's granulomatosis, Microscopic Polyarteritis, and Henoch-Schonlein Purpura, Vasculitis, page 282
 - Multiple Myeloma, page 302

Diabetic Nephropathy

- See also Diabetes Mellitus, page 94
- Epidemiology: Nephropathy in
 - 30 – 50% of type 1 diabetic patients (after ~ 10 – 15 years of disease)
 - 20 – 30% of type 2 diabetic patients – many with overt disease at the time of presentation
 - In both cases is associated with poor glycaemic control, hypertension and ↑ proteinuria
- Definitions:
 - Overt diabetic nephropathy = proteinuria > 500 mg/day in the absence of other renal disease
 - Microalbuminuria:
 - Albumin excretion 30 – 300 mg/day (= 20 – 200 µg/minute). Concentration is not relevant – it is the amount excreted per unit time. Albumin is more specific for nephropathy than total urine protein (normal protein < 150 mg/day – mainly from tubular cells). Normal dipsticks not sensitive enough at this level. Random early morning urine is dependent on concentration. Urinary albumin:creatinine ratio is a useful screening test
 - Marker for endothelial damage elsewhere. Strong association with retinopathy, IHD, etc
 - Prognosis for a diabetic with microalbuminaemia is worse than for HIV!
- Natural History:
 - Type 1 Diabetes:
 - Not usually evident until after 10 – 15 years of disease. If none by 25 years then nephropathy unlikely
 - Once overt nephropathy starts, progresses to ESRF over 5 – 7 years
 - Initial hyperfiltration in about 50% of diabetics (↑GFR by about 25 – 50%). Overtime this reduces and hypertension ensues
 - Type 2 Diabetes: Similar progression to ESRF once overt nephropathy

- Pathology:
 - ↑Intra-glomerular pressure, glomerular hypertrophy, ?deposition of advanced glycosylation end products
 - Glomeruli:
 - Glomerulosclerosis: nodular (Kimmelstiel-Wilson) or diffuse
 - Mesangial broadening with deposition of eosinophilic material
 - GBM irregularly thickened
 - Arterioles show evidence of subintimal arteriosclerosis and hyalinisation
 - Interstitial changes: tubular atrophy and fibrosis
- Look for other renal pathology if:
 - No retinopathy
 - Active urinary sediment
 - Rapid onset nephrotic syndrome
 - Type 2 diabetes
- Management:
 - Glycaemic control. HbA1c < 8.5% delays progression in early phases – not later
 - Anti-hypertensive treatment: All effective. ACE inhibitors are best at ↓ protein and ↓ intra-glomerular pressure. May delay progression even in normotensive patients. Aim to lower blood pressure by as much as possible without creating hypotensive symptoms. Also calcium antagonists (diltiazem and Verapamil → ↓proteinuria)
 - Protein Restriction: Limiting intake may reduce progression. High intake → ↑intraglomerular pressure and hyperfiltration
 - Dialysis: worse prognosis than non-diabetics due to concurrent IHD. Peritoneal dialysis better if CVS instability
 - Transplant: best prognosis in the absence of CV disease. Disease can recur in the graft 5 – 10 years later
- Other renal complications:
 - Urinary tract sepsis. Should be treated even if asymptomatic
 - ↑Risk of pyelonephritis
 - Papillary necrosis. May → macroscopic haematuria or ureteric obstruction
 - Autonomic neuropathy → neurogenic bladder → infection/obstruction
 - Contrast nephropathy: always hydrate aggressively

Systemic Lupus Erythematosus

- Renal involvement common:
 - Clinically apparent in around 50%
 - Histologic lupus nephritis in 100%
 - 5% present with a renal syndrome
- Presentation:
 - Usually heavy proteinuria, nephritic syndrome or RPGN
 - Test for SLE antibodies (see Blood tests in Inflammatory Arthritis, page 270)
 - Most patients have ↓complement
- Histology:
 - Mimics anything!
 - Most severe: Diffuse proliferative glomerulonephritis with crescents
 - Common: membranous pattern, tubulo-interstitial damage
 - Immunofluorescence (IF): extensive deposition of IgG and C3, also C1q, IgA, IgM and fibrin
- See also Systemic Lupus Erythematosus, page 278

Reflux Nephropathy

- See also UTIs in Children, page 221
- Most common cause of end-stage renal failure in children, secondary to vesico-ureteric reflux + infection in infancy
- May not appear till adulthood (ie slowly progressive)
- Investigations:
 - Renal cortical scarring on ultrasound or DMSA scan
 - IVU may show clubbing of calyces
 - Biopsy: chronic interstitial disease with secondary focal glomerulosclerosis
- Treatment: aggressive blood pressure control

Thrombotic Microangiopathy

- Includes Haemolytic Uraemic Syndrome (HUS), Thrombotic Thrombocytopaenic Purpura (TTP) and HELLP Syndrome of Pregnancy (Haemolysis, elevated liver enzymes and low platelets)
- Presentation:
 - Microangiopathic haemolytic anaemia, low platelets and renal and neurological manifestations
 - Renal involvement: haematuria and proteinuria, renal failure in 40 – 80%
- Investigations: Blood film → marked fragmentation of red cells, Comb's test –ive
- Treatment: 90% response to plasmapheresis with or without corticosteroids

Amyloidosis

- A dysproteinaemia that usually presents renally with nephrotic syndrome
- Types:
 - Primary amyloidosis: idiopathic or associated with myeloma. Amyloid protein is part of the Ig light chain. Poor prognosis
 - Secondary amyloidosis: deposition of a different form of protein. Associated with chronic inflammatory or infective conditions (eg Rheumatoid arthritis, Tb, etc)
- Particularly affects glomerular capillary walls, seen with Congo Red Stain

Complications of Chronic Renal Failure

Uraemia

- = Symptom complex associated with severe, near end-stage renal failure (ie GFR < 20 mls/min)
- Leads to:
 - Accumulation of uraemic toxins
 - Anaemia
 - Hyperparathyroidism
 - Metabolic acidosis
- Common symptoms (NB some of these may be due to anaemia alone):
 - CNS: Fatigue, weakness, malaise, ↓concentration, restless legs, insomnia
 - GI: anorexia, nausea, vomiting, gastritis
 - Blood: anaemia, platelet dysfunction (→ bleeding)
 - CVS: hypertension, oedema, pericarditis
 - Skin: pruritis, pigmentation
 - Endocrine: hyperlipidaemia, hypogonadism (→ infertility and amenorrhoea), impotence
- Investigations:
 - Serum creatinine and urea: markers of uraemia but also affected by malnutrition and muscle mass
 - Creatinine clearance: overestimates GFR in severe renal failure as some Cr is secreted in the tubule
 - Albumin: marker of malnutrition and key prognostic factor
 - Ca, PO₄ and PTH: markers of renal osteodystrophy (see Increased Bone Resorption, page 263)
 - HCO₃: degree of metabolic acidosis
 - Anaemia due to ↓erythropoietin (but exclude other causes, eg ↓Fe or folate)
- Management:
 - Protein restriction (but beware malnutrition)
 - Alkalics (eg HCO₃) to control acidosis
 - Aggressive blood pressure control
 - Fluid restriction if pulmonary oedema
 - K restriction and avoiding K increasing drugs
 - Dialysis if these measures fail to control symptoms/signs. See Renal Replacement Therapy, page 217

Anaemia

- Normocytic, normochromic
- Universal in patients with end-stage renal failure (except that it's less common in polycystic disease)
- Secondary to erythropoietin deficiency, plus also ↓ RBC survival
- Also ↓Fe and folate due to dialysis
- Management:
 - Blood transfusion: effective but only temporary benefit. Complications: Fe overload, development of cytotoxic antibodies (→ problems for future renal transplant)

- Synthetic erythropoietin: Very effective, including ↑well-being, exercise tolerance, ↓LV hypertrophy, etc. Most are Fe deficient, so need supplementation (maybe iv). Complications: worsening hypertension

Secondary Hyperparathyroidism

- See Parathyroid, page 101
- Pathogenesis:
 - ↓1,25 (OH)2D3 [calcitrol] from kidneys → ↓Ca absorption and ↑PTH
 - Renal failure → ↓PO₄ excretion → ↑serum PO₄ → ↑PTH
 - ↑PTH in most patients with GFR < 50 mls/min
- Presentation:
 - Pruritis (?soft tissue deposition of calcium phosphate)
 - Bone pain due to calcium resorption
 - Restless legs
- Management:
 - Early replacement of calcitrol (but watch for hypercalcaemia)
 - Phosphate reduction: ↓dietary intake and calcium carbonate (binding agent in the gut → ↓absorption)
 - If these don't control the ↑PTH without causing ↑Ca, then parathyroidectomy (→ hypocalcaemia and requirement for ongoing calcitrol)

Other complications

- Hyperphosphataemia
- Vascular disease
- Chronic fluid overload → LV hypertrophy and ↑ BP

Specific Nephrotoxins

- Aminoglycosides
- Amphotericin
- NSAIDs: → ↓PGs which vasodilate afferent arteriole → vasoconstriction. Compounded risk if already dehydrated, elderly, etc
- ACE inhibitors. Acute renal failure following introduction of ACE → ?renal artery stenosis: already reduced renal flow, ACE dilates efferent arteriole → precipitous fall in GFR.
- All radio-contrasts: ↓risk in at risk patients by maintaining hydration with a saline drip
- Chemotherapy: eg Cisplatin
- Rhabdomyolysis (from trauma, status epilepticus, acidosis, etc):
 - Injury to membrane of skeletal muscle
 - → ↑↑ Ck
 - → Renal failure due to combined effect of nephrotoxic effect of myoglobin, hypovolaemia and aciduria
 - Urinalysis is +ive for blood but no RBCs on microscopy. Urine is dark brown

Kidney Disease

Renal Stones (Nephrolithiasis)*

- Symptoms:
 - Loin pain ⇒ stone in kidney
 - Colic anywhere from loin to groin (may just be the tip of the penis) ⇒ stone in ureter
 - UTI, haematuria, obstruction
- Risk factors:
 - Low urine output (→ drink lots)
 - Hypercalcaemia: hyperparathyroidism, sarcoid, neoplasia, Addison's, Cushing's, hyperthyroidism, Li, could be just due to ↑Vitamin D in summer
 - Hyperoxaluria: high levels of oxalate in chocolate, tea, rhubarb, spinach
 - Hypocitraturia
 - Hyperuricosuria
- Investigations:
 - MSU: RBC, UTI, protein, pH (stones like acid urine)

- Plain X-ray of kidneys, ureters and bladder
- Blood: U&Es, urate, Ca, PO₄, HCO₃
- Management:
 - Pain relief: NSAIDS (but care with ↓renal flow) or morphine
 - ↑Fluid intake
 - Sieve urine to catch the stone for analysis
 - If obstruction or infection → urgent urologist referral

Tubulointerstitial Diseases

- Involve tubules and renal interstitium (not glomerulus)

Acute Tubular Necrosis (ATN)

- Ischaemic:
 - Patchy areas of tubular necrosis (proximal convoluted tubules and straight segments of the loop of Henle) and thinning of epithelial brush border
 - Loss of basement membrane → scarring, loss of architecture → permanent loss
 - Regeneration if not too severe
- Toxin-mediated (e.g. aminoglycosides, radio-contrast agents, heavy metals, arsenic, solvents, also from myoglobinuria from muscle damage):
 - Necrosis is continuous not patchy
 - No loss of basement membrane → epithelium can regrow down the nephron → resolution
- Leads to:
 - Intra-tubular obstruction → ↓GFR. Glomeruli and vessels generally normal
 - Hyaline casts from cellular debris
 - Reduction in sodium reabsorption & loss of medullary concentration gradient → inability to concentrate urine → isoosmolar urine with Na > 20 mmol/L
- Management:
 - Fluid restrict
 - Correct electrolytes
 - Nutrition
 - Avoid nephrotoxins
 - Dialysis if:
 - Severe hyperkalaemia
 - Pulmonary oedema/severe hypertension
 - Symptomatic uraemia
 - Progressive uraemia with oliguria
 - Severe refractory metabolic acidosis
- Lasts 1-2 weeks, followed by gradual improvement in serum urea and creatinine, and diuresis (due to reduced medullary gradient) – monitor to avoid hypokalaemia and hypovolaemia
- Prevent preoperatively by maintaining hydration → maintained renal blood flow. No clear benefit from mannitol, dopamine, frusemide, etc

Acute Papillary Necrosis

- Diabetes
- Also in urinary outflow obstruction → ↑pressure in renal pelvis → ↓perfusion

Acute Interstitial Nephritis (AIN)

- =Intense, often patchy, interstitial inflammatory infiltrate of lymphocytes & monocytes
- Presentation:
 - Similar to RPGN
 - Also skin rash, fevers, eosinophilia of urine
- Glomeruli normal but may be tubular necrosis
- ↓GFR due to tubular obstruction and altered intra-renal haemodynamics
- Associated with drugs (e.g. penicillins - especially amoxycillin, and cephalosporins) – sometimes with infections & systemic diseases. Also NSAIDs – but after months of exposure & severe proteinuria
- Symptoms: 1 – 2 weeks after exposure (ie delayed hypersensitivity): fever, maculo-papular rash, eosinophilia, arthralgia, flank pain
- Urine has pyuria, mild haematuria and mild proteinuria
- Treatment: withdraw drug +/- steroids

Acute Pyelonephritis

- Caused by suppurative infection: E coli, Proteus, Klebsiella, Enterobacter
- From ascending UTI or haematogenous spread of infection (eg septicaemia)
- See Urinary Tract Infections, page 219

Chronic Pyelonephritis

- Not a disease, but a description of what happens to the kidney – it becomes dilated and replaced by fat
- Causes:
 - Recurrent infection
 - Obstructive uropathy
 - Vesicoureteric reflux (especially in kids with malformed vesicoureteric valves. Present in puberty with renal failure – subclinical before that)
 - Kidney stones ($\rightarrow \uparrow$ infection)

Glomerulonephritis

- See also Presentation of Kidney Disease, page 204

Overview

- Variety of conditions \rightarrow inflammatory changes in the glomeruli. If severe enough to cause crescent formation \Rightarrow rapidly progressive glomerulonephritis (see page 215)
- Some forms predominantly present in one way, but any form can present in any way. Can present as:
 - Nephritic Syndrome
 - Nephrotic Syndrome
 - Acute Renal Failure secondary to rapidly progressive GN
 - Chronic Renal Failure
 - Asymptomatic Haematuria or proteinuria
 - Hypertension
- Either:
 - Primary: limited to the kidney
 - Secondary: part of a more widely disseminated immune process
- Systemic diseases that may present as GN:
 - Lupus nephritis: deposits of immune complexes everywhere within the glomerulus
 - Arteritis: Microscopic polyarteritis
 - Amyloid: Nephrotic Syndrome or renal failure. Histology with Congo Red Stain
 - Diabetes
 - Hypertension
- Terminology:
 - Proliferative: proliferation of endogenous glomeruli cells
 - Exudative: infiltration by polymorphs
 - Diffuse: involves all glomeruli
 - Focal: involves only some glomeruli
 - Global: involves the whole glomerular tuft
 - Segmental: involves only part of the glomerular tuft
- Diagnosis:
 - Urine biochemistry: urine sodium > 20 mmol/L (if pre-renal failure then < 20 , ie frantically trying to reabsorb Na)
 - Urine analysis: Blood morphology and casts, protein (usually mild)
 - Ultrasound: exclude obstruction, looking for normal or slightly enlarged kidneys, echogenic (dark on US $\Rightarrow \uparrow$ fluid)
 - CXR: look for Goodpastures Syndrome, Wegener's Granulomatosis
 - Bloods: ANA (connective tissue disorders), ANCA (Anti-neutrophil cytoplasmic antigen \Rightarrow Wegener's Granulomatosis), Anti-dsDNA (\Rightarrow SLE), anti-GBM
- Histology. May see:
 - Glomerula epithelial cells usually have interdigitating foot processes. If they swell, \downarrow gaps between them \rightarrow proteinuria
 - Mesangial cells (supporting framework) are the first to react to injury and the last to return to normal

Management

- Investigations:
 - Urine microscopy
 - 24 hour urine for protein and Cr
 - Serum: U&E, FBC, ESR, CRP, albumin, ANAs, etc
 - Culture: ?blood, throat, ears, skin
 - CXR, US, IVU
 - Biopsy
- Treatment:
 - Prompt referral
 - Keep BP < 145/90
 - Specific treatment
 - Monitor renal function

Clinical and lab features

	Proteinuria		Haematuria		Nephritic	ARF	CRF	Anti-GBM	↓C3	Anti-strep	Anti-IgA
	Asymp-tomatic	Nephrotic	Macro	Micro							
Minimal Change		++++		+							
FSGN	+++	++++		++++			+++				
Membranous	+++	++	+	+++			++				
Post-Infectious	+	+	+	++++	++++	+			+++	+++	
RPGN		+	+	++++	+++	+++	++	++			
IgA	+++	++	+++	++++	+	+	+	+			++
Mesangio-capillary	+	+++	+	++++	+++		++		+++	+	

Minimal Change Disease

- Presentation:
 - Usually nephrotic syndrome, with severe oedema, uncommonly have hypertension and 10% have microscopic haematuria
 - Commonly after an URTI
 - Boys > girls
 - 90% of childhood nephrotic syndrome, 20 – 30% of adult nephrotic syndrome
 - Renal function normal, unless it deteriorates secondary to hypovolaemia
 - Weak association with Hodgkin's Disease
- Investigations:
 - Light Microscopy (LM): glomeruli are normal
 - Immunofluorescence (IF): Negative
 - Electron Microscopy (EM): fusion of foot processes
- Management:
 - Kids: natural history unpredictable:
 - 90% of kids respond to 8 weeks of steroids. If they relapse, respond to steroids again (eg triggered by intercurrent illness). No renal failure but complications of treatment
 - 10% become steroid dependent or resistant → use cyclosporin
 - Steroids less effective in adults, but still reasonable response rate

Focal and Segmental Glomerulosclerosis (FSGS)

- Presentation:
 - Usually nephrotic, can be nephritic
 - Usually microscopic haematuria
 - Accounts for 10 – 20% of nephrotic syndrome in adults
- Investigations:
 - LM: segmental sclerosis of the glomerular tufts. May be ↑mesangial matrix, interstitial fibrosis and tubular atrophy
 - IF: Weakly positive for IgM and C3 (?artefact)
- Management:
 - Poor prognosis: 50% have a five year renal survival
 - Some response but frequent relapse to steroids

Membranous Glomerulonephritis

- Presentation:
 - Nephrotic syndrome, also asymptomatic proteinuria
 - Microscopic haematuria, hypertension, renal impairment
 - 30% of adult nephrotic syndrome, most commonly middle-aged
- Usually idiopathic, but 25% of it is secondary to underlying disease, including:
 - Lung or colon cancer (< 10% of adults presenting with Membranous GN)
 - Infections: hepatitis B, malaria
 - SLE
 - Drugs: penicillamine, gold, high dose captopril
- Investigations:
 - Is autoimmune – but there is no antibody you can measure
 - LM: thickened, irregular capillary loops, spikes in BM with silver stain
 - IF: granular deposition of IgG and C3
 - EM: Subepithelial deposits
- Prognosis: variable – 30% progress to end-stage, 30% improve, and the rest retain stable renal function but with ongoing proteinuria
- Treatment: steroids or cytotoxics for the progressive group

Post-Infectious Glomerulonephritis

- 8 – 14 days following Group A β-haemolytic strep infection of throat or skin, also SBE, osteomyelitis, etc
- Cultures usually negative, strep serology may be helpful
- Presentation: Usually nephritic, may be rapidly progressing → acute renal failure
- Biopsy: usually in adults to rule out a crescentic rapidly progressive GN:
 - LM: mesangial and endothelial cell proliferation + neutrophils. Crescents if severe
 - IF: Usually +ive for granular IgG and C3 deposition
- Treatment: supportive, *not* immunosuppressive. Treat culture positive family members with penicillin
- Prognosis: slow recovery, mild residual impairment in a few

Goodpasture's Syndrome

- GN +/- pulmonary involvement (ranging from pulmonary infiltrate on x-ray to frank haemoptysis)
- Pathogenesis: antibodies against an antigen in the glomerular basement membrane and pulmonary tissue
- Biopsy: Crescents + linear immunofluorescence on the basement membrane
- Can measure serum anti-GBM antibody
- Treatment: immunosuppression (steroids, cyclophosphamide) +/- plasmapheresis
- See also Miscellaneous Lung Diseases, page 92

Mesangial IgA disease (Berger's Disease)

- Most common form of GN. Common cause of recurrent haematuria in young men. Usually more benign
- Presentation, either:
 - Macroscopic haematuria +/- URTI (= Synpharyngeal haematuria)
 - Asymptomatic microscopic haematuria picked up on dipstick testing
 - Nephrotic levels of proteinuria are rare

- Biopsy:
 - LM: **Mesangial** cell proliferation + ↑ matrix formation
 - IF: Mesangial deposits of **IgA** and C3
- Prognosis: only 15 – 20% progress to end-stage renal failure – these are more likely to have proteinuria, hypertension and impaired renal function at presentation
- No effective treatment. Consider immunosuppressive treatment if rapidly progressive
- Similar to Henoch-Schönlein Purpura – but HSP is more widespread, causing purpura (especially buttocks and ankles) and abdominal pain (which may → GI bleeding)

*Mesangiocapillary (Membranoproliferative) GN**

- 50% present as Nephrotic Syndrome
- Biopsy:
 - LM: cellular expansion of the mesangium. ‘Twin track’ BM
 - EM: Subendothelial deposits *or* deposits within the BM

Rapidly Progressive Glomerulonephritis

- What is it:
 - A description not a diagnosis
 - = Acute renal failure secondary to glomerular disease generally with a nephritic presentation.
 - Any form of GN can present in a rapidly progressive form. Generally caused by immune mediated diseases
- ~ Crescentic glomerulonephritis (marker for *severe* RPGN)
 - = Cellular proliferation in glomeruli, and crescent formation.
 - Pathogenesis of crescents: rupture of the basement membrane → fibrin leaks into Bowman’s space, macrophages recruited, epithelioid cells form a crescent. Leads to scarring and fibrosis of glomeruli
- Presentation:
 - Nephritic presentation. Nephrotic range proteinuria is rare
 - → ↓GFR but tubular function OK so Na/H₂O reabsorbed → oedema
 - Systemic features of immune mediated diseases: myalgia, arthralgia, fever, etc
- Investigations:
 - Urine chemistry midway between pre-renal ARF and ATN
 - Light Microscope: Extensive proliferation of cells, numerous crescents, generally without polymorphs
 - Immunofluorescence:
 - Granular IgG and C3 ⇒ immune complex mediated (Post strep, Lupus, etc)
 - Linear IgG ⇒ Goodpastures
 - None ⇒ pauci-immune
- Due to:
 - *Immune complex mediated GN:*
 - Post-infectious GN: e.g. post-streptococcal (rarely crescents, dialysis rarely needed) also staph. See page 214. Has granular IgG plus neutrophils
 - Lupus Nephritis, see page 208. Has granular IgG (plus IgA, IgE, etc)
 - Others, including vasculitis
 - *Anti-glomerular-base membrane diseases* (Goodpasture’s syndrome): See page 214
 - *Pauci-immune:* (ie no evidence of immune deposits, probably cell mediated immune problem):
 - Wegener’s Granulomatosis: Causes GN, URTI, LRTI, non-caseating granuloma, cANCA is highly specific, -ive immunofluorescence, typically older patients. See also Wegener’s Granulomatosis, page 283
 - Microscopic polyarteritis (also joints)
- Prognosis dependent on % of crescents
- Treatment: immunosuppressive (iv methylprednisolone, cyclophosphamide) +/- dialysis

Hypertension

- Histologic changes: intimal fibrosis, hyaline deposition, downstream infarction → progressive scarring, granular surface
- Need to aggressively treat hypertension in people with other risk factors for kidney disease (eg diabetes)
- See Hypertension, page 34

Congenital Abnormalities

- Aplasia: absence of a kidney
- Hypoplasia: usually unilateral, secondary to obstruction of the ureter in utero
- Horseshoe Kidney:
 - 1 in 500
 - Work normally
 - Disturbed renal flow: ureter has to flow over the kidney → recurrent UTI

Hydronephrosis

- Dilation of renal pelvis due to:
 - Obstruction of the pelvo-ureteric junction (often in kids)
 - Big prostates
 - Kidney stones
- Leads to renal failure due to:
 - Chronic interstitial nephritis (as do other things): leucocyte invasion.
 - Atrophy of the collecting ducts and distal tubule (which are relatively hypoxic compared to the glomerulus). However, if the tubule goes, the glomeruli scleroses ⇒ loose whole nephron

Cystic Renal Disease

Adult Polycystic Kidney

- Autosomal dominant: PKD1 loci on chromosome 16 (worse), PKD2 on chromosome 4 (better)
- 1 in 500
- Pathogenesis:
 - Whole nephron blows up → squashes other nephrons → progressive renal failure
 - Cystic lesions in other organs: liver, pancreas, lung
- Presentation:
 - Present with hypertension around 50 → IHD, CVA
 - Vary in severity and onset
 - Usually only moderate proteinuria
 - Kidney's can get very large → impair respiration
- Diagnose with US or CT
- Treatment: slow progression through aggressive blood pressure control

Infantile Polycystic Kidney

- Autosomal recessive
- In mild forms that escape renal failure, is associated with congenital hepatic fibrosis

Cystic Renal Dysplasia

- Due to obstruction of urinary outflow tract prior to the union of metanephric blastema and the ascending ureteral bud
- → Disordered kidney development. Contains bone, smooth muscle, etc but is not a tumour

Simple Cortical Cyst

- Dilation of a single nephron, usually to 5 mm – 1 cm. Most people usually have 3 or 4
- Usually asymptomatic
- If large and rupture → urinary peritonitis

Other

- Infection: Tb and hydatids can present as cystic dilation on US
- Medullary Sponge Kidney: Rare. Dilated collecting ducts

Renal Tumours

Renal Adenoma/Papillary Adenoma

- Most people have one or two
- Associated with renal scarring
- < 5 mm diameter
- Papillary architecture

- No clear cells (if there were then malignant)

Other benign renal tumours

- Renal Oncocytoma: Have oncocytes: cells with abundant mitochondria (pink and granular) – tired epithelial cells. Grossly form a stalate scar
- Renal fibroma
- Angiomyolipoma: composed of fat, smooth muscle and thick blood vessels. Associated with Tuberous Sclerosis

Renal Cell Carcinoma

- 75% of renal epithelial tumours in adults
- Annual incidence 3/100,000
- Risk factors: smoking, obesity, hypertension, unopposed oestrogen
- 3% familial, Von Hippel-Lindau disease
- Clinical features: haematuria, back pain, abdominal mass. Often metastasised before diagnosis
- Histology:
 - Clear Cell Renal Cell Carcinoma – most common
 - Metastasise up the renal vein to the heart → emboli → cannon ball metastasis of the lung
 - Sheets of clear cells
 - 3p25 deletion diagnostic feature
 - Papillary RCC: Better prognosis
 - Chromophobe RCC: Better prognosis, large cells, abundant cytoplasm, small dark nucleus
 - Sarcomatoid RCC: Highly malignant, highly anaplastic

Transitional Papillary Cell Carcinoma

- Present with painless haematuria
- Can cause hydronephrosis, flank pain, and renal colic from clots
- Peak in 6th – 7th decade, M > F
- Derived from epithelium of renal pelvis
- Associated with smoking, analgesic abuse, azo dyes
- Often associated with transitional cell carcinoma of the bladder and ureter

Nephroblastoma (Wilms' Tumour)

- Very aggressive, presents with abdominal mass with or without haematuria. Pain and intestinal obstruction can occur
- 50% present < 3 years, 90% < 10 years, rare in adults
- Derived from metanephric blastema
 - Dark with scant cytoplasm
 - Triphasic histology: epithelial cells, stromal cells, blastema
- Now around 80% cure
- Associated with syndromes:
 - WAGR: Wilms, aniridia, genital anomalies and mental retardation
 - Denys Drash Syndrome: Gonadal dysgenesis, nephropathy
 - Beckwith-Wiedemann syndrome

Other Renal Tumours

- Angiomyolipoma: Benign – but grow and haemorrhage. Composed of fat, smooth muscle and dilated blood vessels
- Juxtaglomerular Cell Tumour: Very rare, benign but causes malignant hypertension

Renal Replacement Therapy

- For end-stage renal failure, characterised by:
 - Severe uraemia
 - Resistant pulmonary oedema
 - Uraemic pericarditis
 - Severe hyperkalaemia
 - Metabolic acidosis
 - Anaemia
 - Renal osteodystrophy

- Usually required if:
 - Cr is 500 – 1000 µmol/L (depending on patient's size)
 - Urea > 35 mmol/L
 - GFR < 10 mls/min
- Wherever possible, the type of treatment is open to patient preference with the aim of home self-care

Principles of Diffusion in Dialysis

- Replaces excretory function of the kidney. Residual kidney function reduces dialysis requirements – but this usually ‘dries up’ over the first few years on dialysis
- Blood is exposed to dialysis solution across a semi-permeable membrane → movement of low molecular weight proteins by:
 - Diffusion
 - Ultra-filtration and convection due to pressure gradient carrying compounds passively in fluid

Haemodialysis

- Indicated for:
 - Acute dialysis
 - Weight > 100 kgs
 - Patient preference
- Contra-indicated:
 - Profound hypotension: dialysis takes half a unit of blood out of the vasculature through the machine → further hypotension
 - Cardiac failure: intermittent nature of dialysis (every 2nd or 3rd day) → accumulating fluid in between times then rapid reduction in fluid. If heart function is dependent on pre-load, then a rapid reduction in circulating fluid → frank failure
 - Inability to establish long term vascular access: a particular problem with diabetics with vascular disease
- Procedure: 3 times a week for 5 to 6 hours, with a dialysis machine, dialysis membrane and dialysate (buffer/electrolyte solution). Access is via an arteriovenous fistula at the non-dominant wrist. There are other options if this fails. Vascular access can thrombose, become infected, lead to high-output failure, etc
- Complications:
 - Hypotension
 - Muscle cramps
 - Bleeding: due to blood loss in dialysis and the anticoagulation necessary to stop clotting in the machine
 - Arrhythmias: due to rapid changes in electrolytes
 - Infections: mainly staph in patients with temporary or tunneled catheters
- CVVHD = continuous veno-venous haemodialysis (used when BP too low for normal dialysis)

Peritoneal Dialysis

- Dialysate introduced into the peritoneal cavity, with diffusion across the peritoneal membrane. Less efficient so requires longer period of dialysis. Good for dialysis while still some kidney function remaining. Easier to learn and lower cost than haemodialysis
- Indicated if:
 - Severe cardiac disease: maintains more stable fluid levels in the body
 - Elderly or frail patients
 - Diabetic patients
 - Patient preference
- Contraindicated if:
 - Previous extensive abdominal surgery: requires adequate peritoneal membrane
 - Greater than 100 kgs: not efficient enough
- Types:
 - Continuous ambulatory peritoneal dialysis: 4 to 5 exchanges each day, each of 2 – 3 litres
 - Automated Peritoneal Dialysis: Machine automatically exchanges through the night (good for kids and people who work through the day)
- Complications:
 - Inadequate dialysis
 - Tenckhoff Catheter problems

- Infection at the exit site and peritonitis (abdominal pain and cloudy dialysis fluid). Usually staph. Intra-peritoneal antibiotics. If G -ive then ?intra-abdominal pathology
- Hydrothorax
- Hyperglycaemia: glucose is used in the fluid to encourage filtration
- Malnutrition

Renal Transplantation

- Treatment of choice. If successful provides full excretory and hormonal function
- 95% of patients and 85% of grafts survival at 1 year. Half life of a graft ~ 13 years
- Not considered if significant co-morbidities
- Types:
 - Cadaveric transplantation: donor and recipient must be ABO compatible with a negative direct cross match test (ie no recipient antibodies which might cause acute rejection)
 - Live Donor Transplants: 25% of transplants. Donors must be investigated to ensure good renal function. Good results due to well donors and better preparation of recipients
- Life-long immunosuppressive therapy is required, using cyclosporin, mycophenolate and prednisone. Combination therapy allows ↓doses → ↓complications
- Acute rejection: oliguria, ↑Cr, fever and swollen graft. May only be picked up biochemically. Most likely within the first 3 months, but can occur at any time. Treated with high dose corticosteroids
- Long term complications:
 - Infections due to immune compromise, including opportunistic infections, eg CMV, EBV, PCP. Prophylaxis during the first 3 months common
 - Malignancy: ↑ skin squamous cell, lymphoma, cervical and Kaposi's Sarcoma – not breast, lung or colon

Ureter

- Congenital abnormalities:
 - Double/bifid ureters
 - Megaureter
 - Hydroureter
 - Usually present with UTIs
 - May have abnormalities elsewhere
- Ureteritis:
 - Associated with generalised UTI
 - May be caused by stones lodging the ureter
 - Rarely caused by Tb
- Transitional Cell Carcinoma:
 - Transitional between squamous and glandular epithelium. Tumours typically papillary/frond like
 - Similar histology to renal and bladder TCC
 - Infiltrates early to retroperitoneum with poor prognosis

Urinary Tract Infections

Investigations

- Dipstick: Under-rated
 - Nitrites (produced by an enzyme in *most* infectious bacteria which breaks nitrates down to nitrites) ⇒ presumptive diagnosis
 - If no leukocytes, nitrates, protein or blood then no infection. Ie high negative predictive value. Positive predictive value only about 30 – 40%
 - Culture should be done (ie not just dipstick) in pregnancy, diabetics, atypical presentations recurrent attacks and non-response to treatment
- Urine Microscopy:
 - Some RBC and WBCs are normal
 - Look for casts, crystals, bacteria. Absence of bacteria not significant (treat empirically)
 - If RBC > WBC then ?stone
- Culture:
 - Bacteruria ⇒ 10E5 colony forming units (cfu) per ml of urine. However, this was set using morning samples in young women via catheterisation ⇒ not much value.

- In kids, a much smaller number may be significant, especially if:
 - In a boy
 - Obtained by catheter. In a supra-pubic aspirate any growth is important
- Most UTIs are caused by a single bug. If multiple organisms then contaminated sample. Bugs can grow in transit → send to lab straight away or refrigerate
- Antibiotic sensitivity: if multi-resistant then usually from Asia where antibiotics are freely available
- Haematuria in 50% - but if asymptomatic → ?bladder carcinoma
- Intravenous pyelogram / urogram (same thing)

Microbiology

	GP	Hospital
E Coli	75%	40%
Coag -ive Staph	7%	6%
Proteus	6%	15%
Klebsiella	3%	12%
Enterococcus	3%	15%
Pseudomonas	1%	6%

- Hospital acquired are more antibiotic resistant
- Pathogenesis: bacterial adherence
 - Uropathic strains: fimbriae – microbial adhesions. Different types in different bugs, and different densities of receptors in hosts → genetic predisposition
 - Catheter adhering strains:
 - Tightly adherent → none grown from urine
 - Thick layer of ‘biofilm’ forms in lumen of catheter containing bugs. Antibiotics can’t penetrate ⇒ change catheter
 - Risk factors: ↑ duration of use (but regular changing makes it worse), female sex, absence of systemic antibiotics, catheter care violations
 - Prevention: avoid catheterisation, lots of fluid, alternative method for bladder drainage (eg condom catheter), closed, sterile bladder drainage, appropriate aseptic technique at insertion

Adults

- Epidemiology:
 - More common in women, older people, and long term care
 - 20% in women 65 – 75, 3% of men
- Definition: Lots of terms with subtle variations in meaning: UTI, bacteruria, bladder bacteruria, asymptomatic, etc, etc
- Presentation:
 - Acute symptomatic urinary infection = urgency, frequency and dysuria (pain on urination). NB urgency and frequency may be unrelated to infection (eg bladder instability)
 - In elderly may present atypically: delirium, falls, immobility
 - Cloudy urine, dark urine (volume depletion), and smelly urine are all normal!
 - Asymptomatic bacteruria = 2 consecutive positive cultures without symptoms attributable to the urinary tract
- Classification:
 - Uncomplicated: normal urinary tract and normal renal function
 - Complicated if:
 - Abnormal urinary tract: eg calculi, reflux, obstruction, paraplegia, catheter, prostatitis, etc
 - Impaired host defences: immunosuppressed, diabetes, etc
 - Impaired renal function
 - Virulent organism (eg Proteus)
 - Male
- Causes of dysuria:
 - Urinary tract infection +/- vaginitis
 - Vaginitis (Candida albicans, trichomonas vaginalis, gardnerella vaginalis)
 - STDs
 - Other: trauma, urethral syndrome
- Treatment:
 - Oral trimethoprim in uncomplicated infections. ↑E coli resistance → will need to change this soon

- Oral quinolones are the main second line agents (eg norfloxacin)
- *Don't* treat asymptomatic positive urine cultures (ie don't test unless symptoms) unless diabetic or pregnant
- Single dose therapy is worse than conventional therapy (7 – 10 days). For adult women, single dose therapy has an odds ratio compared to conventional treatment (5 days or more) of 0.7 for TMP/SMZ (trimethoprim/sulphamethoxazole), and 0.4 for amoxycillin
- Short course possibly as effective as conventional (watch this space)
- Complications: Ascending infection → renal scarring → hypertension, etc
- Prophylaxis:
 - Consider if recurrent infections, eg low dose nightly antibiotics for 3 – 6 months, post-coital antibiotics
 - Bladder emptying at night and after intercourse
 - Topical oestrogen cream if post-menopausal
 - Adequate fluid intake (> 2 litres per day)
- Men:
 - If unknown cause - ?referral to urologist for kidney scan (e.g. stone)
 - Always do urine culture in addition to antibiotics
 - Do swab if discharge

Urethral syndrome

- No bacteria isolatable
- Can be chlamydia (need to do right test)
- Can become very sensitive after a number of infections (general inflammation)
- Acidic urine will hurt more if inflamed → drink lots (dilute urine) and Uracil
- More common in older women

UTIs in Children

- Epidemiology:
 - UTI is common:
 - Males usually have them in their first year, for girls it's on going
 - By age 7, 9% of girls and 2% of boys will have had at least one episode
 - Caused by E coli in over 80% of cases. Others are associated with complicated UTIs or long term antibiotic therapy (eg Candida)
 - Of 1000 kids with UTI:
 - 400 have vesico-ureteric reflux, 100 have renal scars, 10 will develop premature hypertension (eg in older childhood or pregnancy), end stage renal failure in 1
 - 10 – 20 will have obstruction due to urethral valves, VU or PUJ obstruction
 - Greatest risk usually kids < 4 and especially in first year of life
- Risk Factors for UTI:
 - Previous infection
 - Normal anatomy but functional problem: e.g. vesico-urethral reflux (in child, sibling or parent)
 - Structural abnormality: e.g. urethral stenosis/stricture (more common in boys – congenital, trauma or inflammation)
 - Vulvoanitis from poor perineal hygiene
 - Incomplete or infrequent voiding
 - In first year of life, uncircumcised male is 10 times that of circumcised
 - Sexual abuse: only 2% of patients investigated for sexual abuse have UTI as a symptom. UTI without other indications (lesions, bleeding, bruising) is very unlikely to be sexual abuse
 - Antibiotics: disrupt normal peri-urethral flora → predispose to infection
 - Constipation a risk factor: ask about this
 - Indwelling catheter
- Risk factors for VUR:
 - Children with UTI (30 – 40%)
 - Siblings affected
 - Antenatal dilation of the urinary tract (8 – 22%)
 - No evidence that prophylaxis → ↓renal scars (controversial)
- Always have appendicitis as differential diagnosis: can have white cells in urine with appendicitis where appendix is in the pelvis (or elsewhere)

- Symptoms are highly variable:
 - 0 – 2: Fever/hypothermia (?sepsis), lethargy, poor feeding, diarrhoea, vomiting, abdominal distension, failure to thrive
 - 2 – 5: fever, rigours, vomiting, diarrhoea, colic, abdominal pain, some dysuria, offensive urine, haematuria, weak urine stream
 - 5 – 12: fever, rigours, abdominal pain (\Rightarrow upper tract infection), dysuria, frequency, urgency, incontinence, haematuria
 - If systemic illness then \uparrow likelihood of pyelonephritis as well as cystitis. If under one, can have Pyelonephritis without systemic signs \rightarrow if UTI under age 1 then presume Pyelonephritis
- Diagnosis:
 - Urine bag:
 - Wash genitalia before application
 - Test with urine dipstick. If positive, obtain definitive sample with catheter or supra-pubic aspiration (SPA)
 - Do not routinely send bag specimens for culture. Boys have 93% false positive
 - Catheter:
 - For children who can't void on request and where the bladder is in the pelvis (SPA won't work)
 - Uncomfortable. Discard first few mls
 - Growth $> 10E6/\text{litre}$ suggest infection
 - Supra-pubic aspirate:
 - If child too young to obtain an MSU
 - Gold standard: any growth suggests infection (but beware contamination with skin commensals)
 - MSU: discard first few mls
- Exam:
 - Often normal, other than fever
 - Do **blood pressure**, search for loin, abdominal and supra-pubic tenderness, inspect spine and external genitalia, and brief neuro exam of the lower limbs. Check and plot growth
- Management:
 - Admitted for IV antibiotics if:
 - Neonate or immunocompromised
 - Shocked
 - Vomiting frequently (ie oral antibiotics won't stay down)
 - Hospital treatment:
 - Bloods: FBC, blood cultures, electrolytes and Cr. If toxic, consider LP and glucose
 - Antibiotics: *Amoxycillin 50 mg/kg/6hr (max 2g)* (for enterococcus) and *gentamicin 2.5 mg/kg/8hr* (if older than 1 week and normal renal function) to cover everything else.
 - Discharge on oral antibiotics to take total treatment to 10 – 14 days. Then prophylaxis until follow-up
 - Repeat urines to check it's cleared
 - Follow-up:
 - US within, say, 12 hours: checking for obstruction and kidney size. Poor sensitivity for reflux
 - If < 2 years then MCU (Mitrocysto-urethrogram, for reflux \rightarrow risk of scarring) + delayed DMSA scan (eg after 6 months, look for filling defects \rightarrow renal scarring)
 - If > 2 years then delayed DMSA
 - If reflux, then prophylactic antibiotics until out of nappies and 6 months since last UTI
 - Oral Antibiotic treatment:
 - Don't give antibiotics unless a definitive urine specimen has been obtained
 - Antibiotics standard treatment:
 - *Cotrimoxazole 200/40mg in 5 ml, 0.5 ml/kg bd 5 days* (= trimethoprim + sulphamethoxazole – less concern about allergy in kids),
 - *Amoxycillin 15 mg/kg tds po (max 500 mg)* for 5 days
 - *Augmentin 15 mg/kg tds po (max 500 mg)* for 5 days
 - Prophylaxis in children with recurrent infection is common – but duration, drug and dose all remain variable. *Cotrimoxazole 200/40mg in 5 ml, 0.25 ml/kg po od*
 - Repeat urines at conclusion of antibiotics to check it's cleared

- Referral to urologist:
 - Boys: always refer for confirmed UTI, especially if circumcised
 - Girls: At least repeat urines after first UTI to check cleared. Refer after second UTI

Bladder

Interstitial Cystitis

- Usually elderly patients
- Urine sterile
- If severe then intractable pain with decreasing bladder capacity
- Microscopy → ulcerative chronic cystitis
- ?Viral aetiology

Bladder Tumours

Transitional Cell Carcinoma

- Classic association with azo dyes (clothing, plastics, batteries) and smoking
- Present with painless haematuria (ALWAYS investigate painless haematuria)
- Develop as a flat carcinoma-in-situ → papillary tumour → infiltrates
- Management: regular scrapping it out until pathology says its metastatic then cystectomy

Other Bladder Tumours

- Squamous cell carcinoma: common in Egypt due to Schistosoma (parasite). Early infiltration
- Adenocarcinoma: Rare. Resembles large bowel adenocarcinoma. Derived from urachal remnant
- Rhabdomyosarcoma: In childhood. Aggressive but responds to chemo

Urinary Incontinence

- Bladder pressure > urethral pressure = flow of urine
- 8- 34% of community dwelling older people. Women 1.5 to 2 times rate of men
- Only 25 – 50% with urinary incontinence seek medical help
- Physiology:
 - Bladder fills at 25 – 125 ml/hr. Low pressure maintained by reflex arc → detrusor muscle inhibition
 - Conscious sensation to void at 250 – 350 ml, normal capacity 400 – 600 ml
 - Micturition co-ordinated by pontine micturition centre → parasympathetic nerves → S2 to S4 → relaxation of urethral sphincter muscles + contraction of detrusor until < 30 ml left in bladder.
 - Inhibition of pontine centre → voiding.
- Age related changes:
 - ↑Uninhibited detrusor contractions
 - Benign prostatic hypertrophy in men → urinary outflow obstruction → urinary retention
 - ↓Oestrogen in women → ↓urethral sphincter function
 - Miscellaneous: ↓bladder capacity, ↑residual urine, ↑nocturnal urine production
- Impact of age related diseases:
 - D: Drugs (diuretics, anticholinergic side effects → ↓detrusor contraction, sedatives) and Dementia (↓executive function)
 - R: Retention of urine (eg prostate hypertrophy → retention → bladder pressure sphincter pressure)
 - I: Immobility (arthritis, etc), inflammation of bladder (asymptomatic bacteruria), impaction of faeces
 - P: Polyuria (Diabetes, heart failure)
- Established urinary incontinence:
 - Overactive detrusor: Detrusor Instability. Spontaneous contraction when attempting to inhibit voiding (eg stroke, prostate disease) → frequency, nocturia, urgency, urge incontinence. = Bladder instability – common. = **Urge incontinence**. Usually no pathology found
 - Under-active sphincter: If normal bladder then Genuine Stress Incontinence (GSI). In small portion of men with prostate surgery, in women more complex (childbirth trauma, ↓oestrogen, prolapse etc) → **momentary loss of small volume of urine with ↑intra-abdominal pressure (eg cough)**. Occurs in the absence of detrusor activity. Upper urethra slips through the pelvic floor.

- Caused by childbirth, surgery, menopause (→ atrophy of urethral epithelium), masses, prolapse, pregnancy, etc
- Overactive sphincter: anticholinergics, neural damage or prostate problems → retention → overflow incontinence
 - Overflow incontinence: due to over-distended bladder (without detrusor activity)
 - Reflex Incontinence: involuntary loss due to abnormal spinal reflex activity without the desire to void
 - Assessment:
 - History: Screen all elderly people. ‘Have you ever lost control/wet yourself?’ Impact on function, proximity to toilets, fluid intake, medications, etc
 - Exam: neurological, esp. sacral nerve lesions, signs of stroke. Rectal exam (eg sphincter tone, faecal impaction, prostate - although large prostate size does not correlate to urethral obstruction), in women cough induced urine leakage, mobility, eyesight, cognition
 - Investigations: urinalysis to exclude infection, exclude polyuria due to diabetes, urodynamic investigations (measuring micturition pressure and volume)
 - Management:
 - Genuine stress incontinence: pelvic floor exercises, α agonists, oestrogen, surgery
 - Detrusor instability: bladder retraining, bladder relaxants, remove obstruction
 - Overflow: surgery to remove obstruction, intermittent/permanent catheter
 - Other: schedule toileting, pads, etc

Male Genitourinary

Prostate

Anatomy

- Normally 20 – 30 g. Grossly enlarged can be 500g
- Prostate can become infected, hyperplastic or malignant
- Used to be described in lobes. Now described in zones:
 - Anterior zone
 - Transition and central zone: main site of benign hyperplasia
 - Peripheral zone: main site of malignancy. Next to rectum – can palpate on PR
- PR exam:
 - Even if normal, don’t ignore ↑PSA. Cancers can be small or diffuse, or anterior, in an already large prostate → PR isn’t sensitive
 - Nodularity can be detected on PR. This is due to desmoplasia (fibrous reaction) – usually to a *slower* infiltrating cancer

Prostatitis

- Acute:
 - Gonorrhoea most common cause: pain, discharge, haematuria, tender on PR
 - May be infarction secondary to hyperplasia compressing blood supply
- Granulomatous:
 - Tb (rare)
 - Fungal (only immunocompromised)
 - Leakage of prostatic secretion into interstitium post surgery
 - Resolving prostates (hard, knobbly prostate, ↑PSA, mistaken for malignancy). Suspect post surgery, but still need biopsy

Benign Prostatic Nodular Hyperplasia

- Not benign if not treated: → hydronephrosis → kidney failure → death!
- Common: 75% of all men over 75 years of age
- Testosterone ↓ with age → ↑oestrogen → potentiates effect of Dihydrotestosterone (DHT) on the prostate → prostatic hyperplasia
- Morphology: nodular proliferation of ducts, mainly in the central zone
- Histology: epithelial nodules, fibrosis, chronic inflammation, focal infarction
- Management:
 - Transurethral prostatic resection (TURP): always → retrograde ejaculation + risk of impotence and incontinence

- 5α Reductase Inhibitors (blocks Testosterone → DHT). Usually preferred. OK if not acute obstruction

Prostatic Carcinoma

- Occurs in 25% of males over 70 years. (More if include indolent central or transition zone tumours)
- 6% mortality in males
- Predominantly adenocarcinoma occurring in the peripheral zone
- Key histological features: single cell basal layer in duct epithelium, prominent nucleolus, lots of small glands
- Prognosis related to Grade (using Gleason score: 2 is good, 10 is very bad)
- Spreads to pelvic lymph nodes via perineural infiltration
- Prostate Specific Antigen:
 - PSA – a tumour marker. Screening test only. ↑Serum PSA correlates with tumour burden. PSA is a lytic agent that makes seminal fluid runny. If > 4 then do free to bound ratio, and/or follow/refer patient
 - ↑In benign *and* malignant tumours, or inflammation
- Management:
 - Transurethral resection
 - Radiotherapy
 - Radical prostatectomy (selected on basis of tumour bulk and grade (not if very high grade – will already have metastasised). 50% have complications (impotence, incontinence))

Workup of Obstruction from Enlarged Prostate

- Investigations:
 - Cr: checking renal function
 - K and Na: checking renal failure
 - Blood gases for metabolic acidosis
 - PSA
 - Ultrasound: look for distended bladder and hydronephrosis
 - ECG if ↑K: if ECG changes or if K high then may need anti-arrhythmic
- Management:
 - Catheterise: should see K and Cr resolve over a day (depending on remaining renal function)
 - If high K, then insulin + glucose
- Complications of obstruction:
 - Enlarged bladder: hyperplasia of detrusor muscle fibres, ↑space between trabeculated fibres
 - ↑Back pressure in ureter → hydronephrosis
 - ↓Filtration → ↑Cr
 - ↓Function of tubular epithelium due to poor perfusion → ↓active transport of K
 - Acidosis
- Moral: Must act on a distended bladder to protect the kidney

*Prostate Cancer Screening**

- Notes prepared for Public Health Test. Does PSA meet the 6 criteria for a good screening test?
Source: Readings on Closed Reserve
- Is it an important health issue:
 - 2nd leading cause of cancer death in men in the US. In NZ, 800 cases and 400 deaths per year
 - A disease of the very old. 1% < 55 years, 65% > 75 years. Would reducing incidence lead to decline in all-causes mortality?
- Is there a suitable test: PSA test + digital rectal exam. PSA test is reasonably good at detecting pathology, and sensitivity is improving (currently ~ 80%)
- Is the natural history well understood:
 - Wide variety of cancers: from the slow growing, indolent sort to very aggressive
 - Need long enough asymptomatic duration to allow screening at reasonable intervals
 - Screening likely to detect indolent cancers (length bias)
 - Incidence of prostate cancer has increased dramatically since opportunistic screening introduced → treating many cancers that would have remained harmless (ie would die WITH cancer but not BECAUSE of cancer)

- Does treatment at the asymptomatic stage confer positive benefits over later treatment:
 - No firm evidence that radical prostatectomy is better than conservative treatment for asymptomatic cancers
 - For Grade I and II cancers, evidence that conservative treatment is at least reasonably effective
 - Risks of prostatectomy: 30-day mortality of 0.5% + significant levels of ongoing incontinence and sexual dysfunction
 - Assuming 4% rate of detection from screening, 1 in 5000 will die, 1 in 81 will be incontinent, and 1 in 36 will have sexual dysfunction as the result of the screening
 - Conclusion: Screening is good at detection pathology, but don't yet know if treatment is beneficial in net terms
- Infrastructure and cost: of lesser relevance until it can be demonstrated that screening is clinically effective

Penis

- For congenital malformations and paediatric presentations see Penis, page 636
- Epispadias: abnormal opening of urethra on ventral surface
- Fractured Penis: Rupture of corpus cavernosum during erection
- Condyloma: Genital wart. Usually flat. Associated with HPV.
- Erythroplasia of Queyrat (= Bowen's disease): non-invasive cancer of the penis. Premalignant condition. Usually starts in coronal sulcus.
- Squamous cell carcinoma: Very rare, ↑ risk if not circumcised. Early spread to lymph nodes but doesn't disseminate widely

Scrotum

- Steatocystoma: benign sebaceous cysts, hereditary
- Fournier's gangrene: Ischaemic necrosis. Little collateral flow to the scrotum so occlusion → domino effect. Treatment: debridement
- Squamous cell carcinoma

Testes

- For Torsion and Hydrocoele, see Testes, page 636

Infection

- Epididymo-orchitis:
 - Bacterial infection: E Coli, Klebsiella, Proteus
 - In adults also Gonorrhoea
 - Usually self-limiting → antibiotics
 - Key differential: torsion. If in doubt, emergency referral and Doppler US to assess blood flow
- Primary Orchitis:
 - Mumps, Tb, tertiary syphilis
 - Rare

Other

- Spermatocele: dilation of a chord of epididymis: common benign small lump on testis. Translucent to torch
- Haematocoele: Haemorrhage into tunica vaginalis or tunica albuginea (rugby injury, bleeding disorder)

Testicular Tumours

- Incidence 3.5/100,000
- 3% bilateral
- 7% associated with undescended testis
- **Germ cell tumours:**
 - 95% of testicular tumours
 - Derived from germ cells
 - Peak in 15 – 34 year olds
 - Painless swelling of the testis
 - *Seminoma:*
 - 40% of testicular tumours
 - Gross: lobulated pale tumour mass

- Micro: Undifferentiated germ cells + ↑ lymphocytes. Aggressive. Metastasise to inguinal and para-aortic nodes
- Treatment: Orchidectomy via inguinal region (never via scrotum → different lymphatic drainage. Also never biopsy suspected testicular cancers). Very responsive to radiotherapy
- **Teratoma:**
 - 30% of testicular tumours
 - All can recapitulate ectodermal, mesodermal and endodermal tissue
 - Benign teratoma: More common in ovary than testis. 3% chance of malignant change. Mature tissues (usually skin elements – epidermis, hair follicles, etc)
 - Malignant teratoma: metastasise to para-aortic lymph nodes (especially neural cells – very aggressive). Gross appearance – lots of variety. Treatment: chemo +/- radiotherapy. Chemo stimulates cells to mature → still malignant but slower growing → excision of affected lymph nodes
 - **Embryonal carcinoma:** poorly differentiated, resembles adenocarcinoma. Highly malignant. May express tumour marker alpha-fetoprotein
 - **Choriocarcinoma:** Placental tissues (resembles hydatidiform mole). Expresses βHCG → positive for pregnancy test. Contains highly malignant syncytiotrophoblast and cytotrophoblast cells. Responds well to chemotherapy
 - Mixed tumours: Teratoma and seminoma
- **Sex chord/stromal tumours:**
 - **Leydig tumours:** 90% benign. Small brown mass. Present with overproduction of testosterone: precocious puberty or gynaecomastia in post-puberty. Can produce androgens, oestrogen or corticosteroids
 - **Sertoli cell tumours:** Rare. 90% benign. Within seminephrous tubules of the testis. Local infiltration
- **Lymphoma:** Older males, often bilateral, poorly differentiated and poor prognosis
- Testicular tumours present relatively young, lymphoma in older men

Differential of Testicular Swelling

- Ref: Casebook 17, July 2002, Medical Protection Society

	Testicular Torsion	Epididymo-orchitis	Testicular Cancer
Pain	Acute, sudden onset. 30% have lower abdo pain	Usually develops over a day or so	Usually painless – but 30% have diffuse pain or ‘dragging sensation’
Scrotum	Increasing oedema and erythema on affected side	Increasing oedema and erythema on affected side	Testis enlarged. 15% have scrotal inflammation
Palpation	Testis enlarged, exquisitely tender, may ride high	Epididymis usually enlarged	Lump detected in body of the testicle
Age	Usually babies and pubescent boys. Can occur in 20s and 30s	Usually in 19 – 40 year olds	Peak incidence age 25 – 35, but as young as 15
History	May have had previous short acute episodes. Sometimes recent trauma	Sexual activity. UTI	History of undescended testis or family history
Urinary symptoms	90% have normal urinalysis	Dysuria, frequency, urgency, only 10% have discharge	Few in early stages
GI symptoms	Nausea in 1/3. 30% complain of abdo pain	Can be nausea/vomiting	Can be caused by mets
Temperature	Usually normal	May have fever	Usually normal
Cremasteric reflex	Diagnosis confirmed by absence, not excluded by presence	Present	Present

Musculo-Skeletal *

-
- See also Paediatric Orthopaedics, page 618

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History

- HPC:
 - When it started: gradual, *injury* (nature of injury, did it swell straight away, after a day etc)
 - Arthralgia: joint pain without swelling
 - Arthritis: pain and swelling
 - What's happened till now: gradual, fluctuating, etc
 - Now:
 - Site, character, radiation, aggravating and relieving factors
 - Include:
 - Morning stiffness, and how long it lasts (classically inflammatory arthritis)
 - Effect of rest and exercise
 - Sequence of joint involvement
 - Severity:
 - Activities of daily living – what can't they do that they would normally do, use of aids and appliances
 - How far can you walk
 - Night pain: is it keeping them awake (always consider neoplasia and infection)
 - What treatment have they tried: NSAIDS, orthotics, physio, etc
 - Other features of inflammatory arthritis:
 - Systemic: Raynaud's phenomenon, rash, fever, fatigue, weight loss,
 - Eyes:
 - Dry eyes and mouth (\Rightarrow ?Sjogren's syndrome)
 - Red, painful eyes (\Rightarrow ?iritis in seronegative arthritis), conjunctivitis in Reiter's
 - GI: diarrhoea (eg inflammatory bowel disease, scleroderma), mucosal ulcers (eg SLE)
 - Skin: psoriasis, nodules (rheumatoid), ulcers
 - Genito-urinary: dysuria, genital ulcers (\Rightarrow ?Reiter's)
 - Lungs: eg Pulmonary fibrosis in systemic sclerosis, ankylosing spondylitis
 - Kidney: eg Gout
 - Heart: Rheumatic fever,
- PMH
 - Surgery: any operations
 - Medical: any medical problems, especially diabetes, asthma, heart and lung disease
 - Also childhood arthritis
 - Sexually transmitted diseases, especially non-specific urethritis and gonorrhoea
- Drugs, side-effects and allergies (including what the allergy does to them)
- Family history:
 - Especially rheumatoid arthritis, gout, primary osteoarthritis, sero-negative spondyloarthropathies and inflammatory bowel disease. Note age of onset and outcome
 - Also Developmental Dysplasia of the Hip
- Social:
 - Always ask about **occupation**: any potential causes or implications of impaired function
 - Living situation: who else at home, any family living nearby, steps, etc
- Systems review: mainly cardiovascular, respiratory and GI. Also urinary stream in a male with a hip problem (fix the prostate first, otherwise operation \rightarrow urinary retention \rightarrow catheter \rightarrow infection \rightarrow dynamite to a recent hip replacement)

Exam

- General inspection: observe them closely as they walk into the room – pain, gait, getting out of chair
- Joints: gait, look, feel, move
 - Gait
 - Inspection:
 - Need to expose the patient (discretely watch them taking off their clothes – eg undoing buttons), including the joint above and below. Have sheets available to cover the patient. Ensure adequate lighting
 - Compare left with right
 - Look from outside in:

- Skin: scars, redness, swelling, hairs, rashes (eg psoriasis)
- Soft tissue: swelling
- Muscle: wasting \Rightarrow chronic disuse, surrounding inflammation or nerve damage
- Bone and joint: deformities – usually a sign of destructive arthritis, also subluxation and dislocation
- Other inspection: eg nails
- Palpation:
 - Warmth
 - Tenderness (watch their face)
 - Evidence of:
 - Synovitis: soft and boggy swelling
 - Effusion: can shift within the joint
 - Bony swelling (eg osteophyte formation or subchondral bone thickening): hard and immobile
- **Move** – Range of movement:
 - Better information from passive rather than active movement
 - Fixed Flexion Deformity = Limited extension
 - Fixed Extension Deformity = Limited flexion
 - Stability: attempt to move the joint in abnormal directions
 - Joint crepitus: grating sensation or noise from the joint
 - Measure angles with a goniometer. Anatomical position = 0°
- To finish:
 - Special tests
 - Joint above and below
 - Distal pulses
 - Neurology
 - Xray and/or aspirate
- Think: acute, chronic, impact on function, systemic effects
- Is it broken?
 - Can they walk/use it at all? If they can hobble, fracture less likely
 - Bony tenderness increases likelihood of fracture

Radiology

- Check name and date
- Check quality and that film covers the pathology you want

Rules of 2

- **ALWAYS** take 2 views at 90%
- Include 2 joints: one above and one below:
 - Especially in paired bones of arm and leg. If there is a fracture with shortening, there will also be dislocation
 - Need to assess rotation relative to joint
- Sometimes need to Xray 2 times. Eg May not see a scaphoid fracture until 10 – 14 days later (will see it with a bone scan after ~ 24 hours)
- Sometimes need to do opposite side to get a good idea of normal – especially if dealing with a complicated joint in a child with lots of epiphyseal plates around. Don't do it routinely due to \uparrow radiation

Describing a fracture

- Which bone
- **Site** (where on the bone):
 - For a femur it can be capital (through the head), subcapital (below the head), transcervical (through the neck), intertrochanteral, supracondylar, at the junction of the proximal and middle thirds, etc
 - Diaphysis: mid-portion or shaft of a long bone. Outer cortex and inner medulla
 - Epiphysis: Ends of long bones
 - Metaphysis: rapidly growing trabecular bone underlying the growth plate

- **Type:**
 - Greenstick: only the convex side of the injured cortex is disrupted, transverse fracture. Only in kids (higher collagen content and less mineralisation). Can also present as:
 - Bowing of a long bone
 - Buckle: fracture around the epiphysis if the force was along the axis of the bone
 - Transverse: force at 90% to bone ie direct blow (\Rightarrow also soft tissue injury). Stable when reduced
 - Oblique: force at 90% while weight bearing (net vector is oblique). Slips out of reduction
 - Spiral: rotatory force – twisting. Don't need big force
 - Comminuted (> 2 pieces)
 - Epiphyseal: described by Salter-Harris Classification: from I to V (most complex). II most common (break through epiphysis with a small chip of bone)
 - Intra-articular
 - Segmental: 2 breaks separated by a section of normal bone. Big force required
 - Stress: fractured bone trying to heal itself and refracturing, etc. May be visible on X-ray, will be visible as a hot spot on bone scan
 - Avulsion: ligament tears off bone
- All fractures can also be:
 - Pathological
 - Simple or compound (bone communicates with air). If compound then Gustilo Classification from I (minor) to III (extensive)
- Further description of the fracture: LARD
 - **Length:** is it shortened or distracted (lengthened, eg soft tissue falling into the gap at the time of impact)
 - **Angulation:** degree and direction. Described as the distal relative to the proximal portion when in the anatomical position. Medial is varus, lateral is valgus
 - Rotation
 - **Displacement/Translation:** are the two ends aligned? Range from 0 to 100% displaced, and direction of displacement
- Associated symptoms: eg
 - Compound wound (eg may see **air** in soft tissue)
 - Compartment syndromes
 - Foreign bodies, etc
- Types of joint injury:
 - Sprain: tearing of ligaments
 - Subluxation: partial loss of congruity of the articular surfaces
 - Dislocation: complete loss of congruity of the articular surfaces
 - Fractured dislocation

Fractures

Management of Fracture of the extremities

- Immediate assessment:
 - Straighten any displaced fracture to allow adequate blood flow
 - Examine for fractures
 - Examine for dislocations
 - Compartment syndromes
 - Look for vascular injuries: Hard to assess for vascular injuries when SBP is less than 90 mm Hg
 - Look for nerve injuries
- Goals of fracture management:
 - Upper limb: restore function
 - Lower limb: obtain and maintain alignment \rightarrow restore alignment, angulation, rotation and length
- Principles:
 - Reduce severe deformity as soon as possible if it is causing soft-tissue or neurovascular compromise
 - Open fractures \rightarrow antibiotics
 - Assess for conservative or surgical treatment
 - Management is a tension between immobilising it long enough to enable union, and short enough to stop stiffening/arthritis of immobilised joints

- Methods:
 - Immobilise. However, casting → muscle atrophy, stiff joints, OA, DVT
 - Reduction: by manipulation, traction or open reduction
 - If it involves joint articulations: open reduction and fixation (especially if displaced) so that early movement can occur, otherwise secondary OA
 - Internal fixation: plates, nails (Kuntscher) or wires (Kirschner)
 - External fixation: screws into bone with external bracing
- Rules for manipulation to obtain closed reduction:
 - If you manipulate, then re-xray now
 - Review early (eg after 1 week). Can't re-manipulate after this should that be necessary
- Indications for surgery:
 - Failure to obtain *or* maintain closed reduction, or where closed reduction has high failure rate (eg fractured neck of femur)
 - Intra-articular fracture (especially if > 1mm displacement after reduction). Failure to operate leads to:
 - Short term: irritant effect of synovial fluid → non-union
 - Long term: pain, arthritis, instability
 - Arterial compromise
 - Open fracture
 - Pathological fracture
 - Multiple injuries
 - Segmental fracture
- Risks of surgery:
 - ↑Soft tissue damage
 - ↓Wound healing
 - Anaesthetic risks
 - But potentially quicker recovery

Healing of Fractures

- Stress fractures occur in:
 - The elderly with osteoporosis
 - Metabolic bone disease
 - Very active runners/sports people (eg tennis, squash)
 - Never in kids
- Factors improving remodelling:
 - Young age
 - Long bones (for example, cf carpal bones)
 - Close to growth plate
 - If angle is in the principle direction of movement (ie posterior or anterior angulation of the radius, given this is in line with flexion and extension of the wrist)
- Factors impairing healing:
 - Movement
 - Non-union
 - Infection
 - Poor blood supply
 - Comminuted
- Rule of thumb for fracture healing:
 - Upper limb: 4 – 6 weeks (kids at shorter end, adults at longer end, etc)
 - Ankle: 6 weeks (close to a joint so want to mobilise early)
 - Tibia and femur: up to 12 weeks
 - Other specific times for some fractures
- When to mobilise:
 - Stable fractures should be mobilised soon
 - Unstable fractures should be stabilised before mobilising
- Patient advice:
 - If the limb distal to a cast ever goes blue, becomes painful or tingles, elevate it for $\frac{1}{2}$ an hour and if no improvement return immediately (not the next day). Remove cast and assess for improvement. If no improvement then urgent opinion

- When to start mobilising

Complications of Fractures

- Joint stiffness: Cartilage requires motion for nutrition. If held in one position → risk of cartilage deterioration
- **Delayed Union:**
 -
 - Presents as pain + movement at fracture site with stress
 - Normal union times

	Upper Limb	Lower Limb
Callus Visible	2-3 weeks	2-3 weeks
Union	4-6 weeks	8-12 weeks
Consolidation	6-8 weeks	12-16 weeks

 - If these times prolonged “delayed union” is likely
 - Causes: Severe soft tissue damage, inadequate blood supply, infection, insufficient splintage, excessive traction
 - Clinically: site tender, painful if subjected to stress, x-rays still show visible line
 - Treatment: needs to be reviewed if no bridging callus by 3 months. Need internal fixation and bone grafting
- **Non Union:**
 - Non-union is likely if delayed union is not treated
 - Presents as non-painful movement at the fracture site
 - Causes: Too large a gap (bone missing, muscle in way), interposition of periosteum
 - Clinical: Painless movement at fracture site. Xray shows smooth and sclerosed bone ends or excessive bone formation
 - Treatment: Not all cases need treating eg scaphoid, otherwise fixation and bone grafting necessary.
- **Infection** in open fractures:
 - → Osteomyelitis, slow union and increased chance of refracture
 - Clinical: History of open fracture or operation on closed fracture. Wound inflamed. Systemic signs of fever
 - Treatment: All open fractures require prophylactic antibiotics and excision of devitalised tissue. If acutely infected, surrounding tissues should be opened and drained + antibiotics.
- **Malunion:**
 - When bone fractures join in an unsatisfactory position i.e. unacceptable angulation, rotation or shortening
 - Aetiology:
 - Failure to reduce a fracture adequately
 - Failure to hold reduction while healing proceeds
 - Gradual collapse of comminuted or osteoporotic bone
 - Signs and symptoms: Usually obvious eg. Unusual bone alignment, x-ray
 - Treatment:
 - If detected before union complete angulation may be corrected by wedging of plaster
 - Forceful manipulation under anaesthetic
 - Osteotomy if union complete and deformity severe
- **Compartment Syndrome:**
 - Elevated pressure in an enclosed space (eg muscle compartment) can irreversibly damage the contents of that space (eg ischaemia)
 - Major causes: Processes constricting the compartment or increasing the contents of the space:
 - Compressive bandages
 - Tight cast
 - Haemorrhage and oedema after fracture
 - Closure of fascial defects
 - Muscles once infarcted are replaced by inelastic fibrous tissue (eg Volkmann's Ischaemic Contracture of the forearm compartment after humeral supracondylar fracture). Most sensitive test is passive extension of the muscles. Can still have arterial flow through the compartment while muscles are becoming ischaemic
 - Signs and symptoms (The 5 p's i.e.):
 - Pain
 - Paraesthesia

- Pallor
- Pulselessness
- Paralysis
- Diagnosis: Pressure $> 30 - 40\text{mmHg}$ (using needle manometer etc) and/or MRI
- Treatment: Remove bandages, etc, consider decompression with a fasciotomy if pressure high, with wound left open for 5 days
- **Avascular Necrosis:**
 - Aetiology
 - Rare
 - Focal subchondral infarction → collapse of necrotic segment → joint deformity → arthritis
 - Common in bones that derive most of their blood supply from the medullary cavity
 - Mainly femoral head, also knee, scaphoid, head of talus
 - Gross: infarct is yellow, opaque and chalky with rim of hyperaemic fibrous tissue
 - Causes:
 - Trauma (eg subcapital fractured neck of femur)
 - Secondary to corticosteroid treatment
 - Nitrogen embolisation in divers (\rightarrow Bends \rightarrow Caisson disease)
 - Sickle cell disease
 - Alcoholism
 - SLE
 - Infective endocarditis
 - Radiation
 - Diabetes mellitus
 - Signs and symptoms:
 - Joint stiffness
 - Pain in or near joint
 - Local tenderness
 - Restricted movement
- Other complications of fractures:
 - Venous thromboembolism: injury patients are at risk due to immobility, leg injury, etc
 - Skin necrosis
 - Pressure sores
 - Fat embolism: typically day 3 – 10. Confusion, sudden SOB, hypoxia. Immediate ICU management
- Charcot's Joint = neuropathic joint:
 - Causes: diabetic neuropathy, tabes dorsalis, cauda equina, leprosy
 - Gross disorganisation of the joints (even dislocation) following repeated minor trauma \rightarrow recurrent stress fractures that aren't felt due to neuropathy

Soft Tissue Injury

Prevention of Sport Injuries

- Proper warm up
- Cooling down
- Protective equipment
- Good technique and sensible training schedules

Ligament Injuries

- Sprain: partial tear of ligament or joint capsule but the joint is still stable. Site of tear is tender and there may be bruising. Symptomatic treatment and protection from stress until healing is complete
- Partial Rupture: If rupture is incomplete, treat conservatively (ranging from rest and analgesia to casting for 6 weeks). Recurrence common
- Complete Rupture: Poor healing as scar tissue is not as tough as the ligament. May attempt surgical repair – but it may not help

Tendon Injuries

- Due to sudden, violent contraction
- Most common is Achilles Tendon Rupture. See Lower Leg and Foot Injury, page 257

- Can also rupture long head of biceps and supraspinatus
- Other tendon injuries:
 - Paratendonitis: Inflammation due to friction of the paratendon (fatty tissue in the fascial compartment through which a tendon runs). Usually Achilles or wrist tendons. Try good footwear or rest in a splint. Steroid injection (but not into the tendon itself) may be effective. NB steroid injections around the Achilles are controversial – may weaken the tendon
 - Tendonitis: irritation/tearing of fibres due to repeat trauma. Pain worse on contraction. Rest + NSAIDs

Frost Bite

- Formation of ice-crystals in the skin and soft tissues when temperature < -3 °C
- Presentation: tissue is pale, grey, and doughy – or frozen solid. May develop without person knowing
- Treatment:
 - Warm slowly – this will be painful
 - Blisters may form over several days. May develop blackened shell as blisters burst
 - Dry, non-adherent, strictly aseptic dressings and prevention of further trauma (tissues are numb)
 - Recovery takes weeks. Surgery may be required

Contusion

- Characterised by direct trauma to a muscle group with subsequent pain and swelling due to bleeding within the muscle
- Management:
 - Rest, ice, mild compression and elevation to control swelling, bleeding and pain
 - Intermittent icing for up to 48 hours
 - Maybe NSAIDS – but may increase the bleeding
 - Exclude other injuries, including compartment syndrome
 - Once swelling has settled, aim is to restore function, beginning with gentle isometric muscle exercises

Lacerations

- Torn, ragged wound
- Treat for bleeding: expose wound to assess for blood loss, cover, direct pressure, elevate, pad and bandage
- If severe then sutures. However, muscle divided transversely will not hold sutures well enough to stop muscular contraction pulling the edges apart

Enthesitis

- Inflammation at the site of attachment of bone to a tendon, ligament or joint capsule
- Elbow: See Tennis and Golfer's Elbow, page 246. Treatment: rest and strapping. Steroid injection if severe
- Plantar Fasciitis:
 - Insertion of the tendon into the calcaneum
 - Pain on standing and walking
 - Is isolated, or with sero-negative arthritis
 - Treatment: heel pads, reduced walking, steroid injection

Chronic Compartment Syndrome

- Caused by ↑ tissue pressure in a closed fascial space → ↓ circulation to muscles and nerves
- Presentation: pain or deep ache over compartment. Usually after prolonged exercise. Usually bilateral. May have palpable muscle hernias
- Diagnosis: difficult. Elevated pressure within the compartment during/after exercise with slow return to resting pressure
- Treatment: decrease exercise (→ ↓ muscle bulk) or elective fasciotomy (can affect muscle strength)
- 'Shin Splints': Shin soreness in unfit runner: can be due to a combination of muscle tears, mild anterior compartment syndrome or stress fracture

Causes of Non-traumatic Limb Pain

- Muscle disease: polymyositis, polymyalgia rheumatica, tendon inflammation, compartment syndrome
- Bone disease: osteomyelitis, osteomalacia, osteoporosis, tumours
- Vascular disease: Arterial or venous (eg DVT)

- Neuropathy: nerve entrapment, neuropathy

Nerve Injury

- See Common Peripheral Nerve Lesions, page 123 for common peripheral nerve injuries
- Types:
 - Neuropraxia: transient loss due to external pressure
 - Aconotmesis: loss of function for weeks/months due to more severe compression. No loss of neuronal continuity
 - Neurotmesis: nerve division. No recovery without surgical repair
- Mechanisms: Division, stretching, crushing, ischaemia alone or in combination
- Common sites:
 - Upper Limb:
 - Median nerve: hand through window
 - Ulnar nerve at elbow: fracture or pressure
 - Radial nerve: cuts around the elbow
 - Digital nerve: finger cuts
 - Brachial plexus: Downward pressure at the shoulder damages the upper cord, upward pressure damages lower cord
 - Cervical nerve roots: compression of vertebrae
 - Lower Limb:
 - Common peroneal nerve: damage at the neck of the fibula
 - Lumbar nerve roots: prolapsed discs
 - Sciatic nerve: hip dislocation
- Management:
 - Immediate primary suture: if clean cut
 - Secondary suture: Clean and debride then suture two weeks later
 - Cable Grafts: if long area of damage: graft from another nerve

Back and Neck

- Spondylosis = degenerative
- Spondylitis = inflammatory

History

- Onset
- Where is it situated
- Sudden or gradual
- Radiation
- Aggravated by movement, coughing or straining
- Effect of rest
- If musculoskeletal then usually well localised and aggravated by movement
- If progressive and unremitting consider osteoporosis (with crush fractures), osteomalacia, or neoplasia (secondaries, leukaemia or myeloma)
- General health, weight loss, fever, sphincter disturbance

Exam

Inspection

- Look at belt line: is the pelvis horizontal.
- Scoliosis:
 - If postural (eg do to a short leg) will correct when sitting down.
 - If pathological will hump to one side when they bend forward
- Dominant hand will usually have a lower shoulder ("Which hand do you sign your name with?")
- Check shape, scars, lumps, muscles spasms, etc

Neck

- Examination: Look while sitting
- Feel. Place forearm against shoulder and fingers on forehead to stop them tensing when you push on the spine. Feel down cervical spine

- Test movement actively. Extension, flexion and lateral flexion normally 45°. Left and right rotation normally 70°. If you need to measure, then measure from the sternal notch to the chin in each position
- If neck pain, check neurology in arms

Thoracolumbar Spine and Sacroiliac Joints

- Look for deformity – inspect from both back and sides. Look for scoliosis, eg from trauma, developmental abnormalities, vertebral body disease (eg rickets, Tb) or muscle abnormalities (eg polio)
- Feel each vertebral body for tenderness and palpate for muscle spasm
- Gently tap spine with closed fist: severe localised tenderness suggest infection/tumour/trauma → do x-ray
- Movement:
 - Flexion (touch toes), extension, lateral bending (slide hand down side of leg as far as possible without bending forward)
 - Rotation: sit on stool (fixes pelvis) and rotate each direction
 - Schober's Test: for lumbar flexion. Make a midline mark at the level of the posterior iliac spine (about L5). Make another mark 5cm below and 10 cm above the first mark. Ask the patient to touch their toes. An increase of < 5cm between the upper and lower marks ⇒ limitation of flexion
 - Lasegue's Sign for lumbar disk prolapse: passive lifting of straight leg is limited by pain as Sciatic nerve is stretched → root pain
 - Palpate sacroiliac joints while they lie on their stomach
- Special tests:
 - Heel/toe walking, squatting may reveal weakness
 - Measure limb girth for wasting
 - Nerve tension tests: straight leg raising, sciatic stretch, femoral stretch
- Always test legs:
 - Neuro: sciatic pain, sensation, power, reflexes
 - Pulses
- Abdominal: Is this a bleeding AAA? Pancreatitis radiating to the upper back?

Xray Interpretation (ABCS)

- Alignment: anterior and posterior lines should be smooth curves
- Bones: Assess each vertebrae – trace each round body. Processes and facet joint may be obscured. Look for osteophytes
- Cartilage and joints: discs should be similar and even. Facet joint dislocation only occurs in association with severe damage to vertebrae
- Soft tissue: disruption of shadows
- Non-traumatic injuries very rarely have positive findings on plain X-ray

Neck and Radiating Arm Pain

Cervical Spondylosis

- Spondylosis is the most common disorder of the cervical spine. Universal in patients over the age of 40 but seldom causes symptoms
- Intervertebral discs degenerate and flatten (ie not synovial ⇒ not OA)
- Bony spurs appear at the anterior and posterior margins of the vertebral bodies. Posteriorly, these may encroach upon the intervertebral foramina, causing pressure on the nerve roots
- Clinical features:
 - Neck pain and stiffness, usually gradual onset and worse on getting up
 - Pain may radiate widely, to occiput, scapular muscles and down one or both arms
 - May be paraesthesia, weakness and clumsiness
 - Weakness of the legs or bladder disturbance suggest cervical cord compression
 - The appearance is normal. Tenderness occurs in the posterior neck muscles and scapular region, all movements are limited and painful
- Differential Diagnosis:
 - Thoracic Outlet Syndrome: pain in the ulnar forearms and hand
 - Carpal Tunnel Syndrome: pain and paraesthesia are worse at night. Nerve conduction is slowed across the wrist
 - Rotator cuff lesions: pain is like one of a prolapsed cervical disc, but shoulder movements are abnormal and there are no neurological signs

- Cervical tumours: Symptoms are not intermittent and x-ray may be abnormal
- X-ray: Cervical disc spaces are narrowed. Corners of vertebrae have osteophytes. Oblique views may show encroachment of the intervertebral foramina
- Treatment:
 - Heat and massage are soothing
 - Neck collar is the most effective treatment during painful attacks
 - Physiotherapy
 - Operation is seldom indicated but if necessary then anterior fusion is appropriate

Prolapsed Cervical Disc

- May be precipitated by local strain or injury, esp. sudden flexion and rotation
- May be a predisposition abnormality of the disc with increased nuclear tension
- Prolapsed disc may press on:
 - Posterior longitudinal ligament, causing pain and stiffness
 - Nerve roots, causing pain and paraesthesia in one or both arms
- Usually occurs above or below the 6th cervical vertebra, nerve roots are C6 and C7
- Presentation:
 - Usually acute in onset and more severe than those of neck strain
 - Pain may be referred into the scapula, shoulder or hand and there may be associated paraesthesia
- Differential:
 - Cervical spine infections, pain is unrelenting and local spasm severe, x-ray show erosion of the vertebral end-plates
 - Cervical tumours, neurological signs are progressive and x-rays show bone destruction
- X-rays may show slight narrowing of the disc space. Disc itself is best seen on MRI
- Treatment:
 - Rest: in a collar to prevent unguarded movement
 - Reduce: traction may enlarge the disc space
 - Remove: if symptoms are severe enough the disc may be removed

Back Pain

Sources of Pain

- Local: processes compressing or irritating nerve endings, e.g. fractures or tears. If it does not vary with change in position then ?spinal tumour or infection
- Pain referred to spine: arises from abdominal or pelvic viscera. Often unaffected by position of spine
- Pain of spinal origin: Upper lumbar refers to groin or anterior thighs. Lower lumbar refers to buttocks, posterior thighs or calves/feet
- Radicular back pain: sharp and radiates from spine to leg in territory of nerve root. Coughing, sneezing or voluntary contraction of abdominal muscles often elicits radiating pain. Increase pain in postures which stretch the nerve root (e.g. sciatic nerve – L5 & S1 - when sitting as it passes posterior to hip, but not femoral nerve – L2 – L3 as it passes in front of the hip)
- Pain associated with muscle spasm: accompanied by abnormal posture, taut para-spinal muscles and dull pain
- Very hard to differentiate lower back pain → cheat and call it lumbar spine dysfunction!

Classification

- Pathological (5%): infection, inflammation, metabolic bone disease, neoplasm
- Referred (5%): Abdominal or pelvic organs
- Mechanical (95%):
 - Muscle/ligament injury
 - Intervertebral disc injury
 - Spondylolysis and spondylolisthesis

Age

- Children: congenital or developmental disorders, infection, primary tumours (ie don't ignore back pain in children)
- Younger adults: disc disease, spondylolisthesis, acute fractures
- Older adults: spinal stenosis, metastatic disease, osteopenic compression

Injuries

- Hyperflexion → wedge fracture around T12 – L2
- Shearing → anterior or posterior displacement, intervertebral ligaments torn
- Hyperextension: tears longitudinal ligaments, widens anterior disk space
- Axial compression: squeezes T4 – L5 → disc squeezes out and disrupts longitudinal ligaments
- Spondylolysis: defect/fatigue fracture in the pars interarticularis. Most common cause of low back pain in children and adolescents. Defect in the neck of the ‘Scottie dog’ on oblique x-rays

Mechanical Back Pain

- No obvious pathology – following trauma or progressive onset. But major cause of people off-work etc
- Spinal movement is complex ⇒ there are many components that could cause pain
- Not related to old age: most common in 25 – 60 year olds
- Patterns:

	Disc Pain	Facet Joint Pain	Nerve Root Pain	Spinal Stenosis
Location of pain	Worst in back. May spread to buttocks or legs	Worst in back. May spread to buttocks or legs	Mainly in legs, may be some in the back	Worst in the legs: heaviness/aching
Pattern	Intermittent or varying intensity	Always intermittent	Usually constant	Intermittent, occurs with activity
Pain worse with:	Sitting, bending forward	Bending backwards, standing/walking for long periods	Sitting and bending, and by backwards movement if acute	Worse with activity
Pain better with	Bending backwards, walking better than standing better than sitting	Bending forward	Lying face down, or on back with legs drawn up	Bending forward, sitting
Exercises	Face down, push up with hands arching spine	Lie on back, knees to chest. Pelvic tilt ($\rightarrow \uparrow$ tilt on walking)	Lie on back on the floor with knees over a chair	Sit ups to strengthen abdominals

- *Lumbar Spondylosis:*
 - Degeneration of joints and of intervertebral discs
 - Gel of nucleus pulposus shrinks and loses compliance causing circumferential bulging of annulus fibrosis.
 - Osteophytes may form
 - Most common sites are L5/S1 and L4/L5
 - Facet joint syndrome – secondary osteoarthritis of the facet joints. Pain worse bending backwards
 - Presentation: midline pain radiating to groin or buttock, worse towards the end of the day, aggravated by coughing or sneezing. Straight leg raising is normal
 - Treatment: analgesics, physio, spinal fusion
- *Acute lumbar disc prolapse:*
 - Nucleus pulposus extrudes into a fissure in the annulus and bulges beneath the posterior longitudinal ligament:
 - Pressure on ligament → back ache
 - Pressure on dural envelope of the nerve root → pain referred to lower limbs (sciatica)
 - Compression of nerve root → paraesthesia and muscle weakness
 - Posture: stand forwards and sideways tilt
 - Sudden onset lasting for hours/days. Local tenderness and loss of spinal mobility
 - Differential:
 - Inflammation (eg due to Ankylosing Spondylitis or Tb)
 - Vertebral tumours → constant pain
 - Nerve tumours cause sciatic but constant pain
 - X-ray to exclude bone disease. CT/MRI best for localising the lesion
 - Treatment:

- Rest: most resolve spontaneously
- Reduction: continuous bed rest and pelvic traction for 2 weeks
- Removal: if cauda equina compression, persistent pain after 2 weeks or neurological deterioration
- Rehabilitation: isometric exercises and advice on bending/lifting
- *Spinal and root canal stenosis:*
 - Due to progressive loss of disc height, OA of facet joints, posterior osteophytes
 - Rarely → neurogenic claudication (nerve root ischaemia) when walking. Due to ↓ blood flow to the cauda equina (whose metabolic needs ↑ on walking)
 - Differential of vascular and neurogenic claudication:

Activity	Vascular Claudication (no foot pulse)	Neurogenic claudication
Walking	Distal → proximal pain, calf pain	Proximal → distal pain, thigh pain, symmetrical, tingling nerve pain
Uphill walking	Symptoms develop sooner	Symptoms develop later (leaning forward opens facet joints →↑blood flow)
Rest	Relief with standing	Relief when sitting or bending
Bicycling	Symptoms develop	Symptoms do not develop
Lying flat	Relief	May exacerbate symptoms
Treatment:	Vascular bypass	Usually have foot pulses. Rest, Decompressive laminectomy

- *Spondylolisthesis:*
 - Anterior or posterior displacement of a vertebrae with or without preceding injury (usually L5 slides forward on S1)
 - Can be congenital (eg defect of articular processes) or acquired (trauma, OA of facet joints, pathological, fracture of the neural arch, elongation of the pars interarticularis)
 - Requires bilateral interarticular defect → instability
 - X-ray (AP and lateral) if:
 - < 20 years or > 50 years
 - Suspicious pain
 - Worse at night and in morning (inflammation, infection, tumour)
 - Neurological signs (→ CT/MRI)
 - Management:
 - Conservative: lumbosacral support, exercises to build extensor and abdominal muscles
 - Surgery: Nerve release and spinal fusion
- Other non-mechanical back-pain:
 - Sway Back: pregnancy: altered spinal posture and ligamentous laxity. Conservative treatment
 - Osteoporotic: painless or agonising localised pain that radiates around ribs and abdomen. Caution with spine physio: mechanical lever arm forces on vertebrae are very strong → easy damage
 - Psychogenic pain is a contributing factor in some. Look for signs of secondary gain

Localisation of Lumbar Root Nerve Entrapment

Nerve Root	Usual prolapse	Sensory Changes	Reflex Loss	Weakness
L2	L2/L3	Front of thigh	None	Hip flexor and adductors
L3	L2/L3	Inner thigh & knee	Knee	Knee extension
L4	L4/L5	Inner calf	Knee	Knee extension
L5	L4/L5	Outer calf, upper inner foot	None	Inversion, dorsiflexion of toes
S1	L5/S1	Lateral borders/ sole of foot	Ankle	Plantar flexion

Red Flags

- Continuous or progressive pain which doesn't change with movement
- Fever (e.g. infection)

- Bowel/bladder involvement (sacral roots)
- Also:
 - Young (< 20) or old (> 55)
 - Violent trauma: MVA or fall from a height
 - Bilateral or alternating sciatica
 - Weak legs
 - Weight loss
 - ↑ESR
 - On oral steroids
 - IV Drug use
 - Pain with movement in all directions
 - Localised bony tenderness
 - Past history of neoplasia
 - CNS deficit at more than one root level or bilateral
- If no red flags then investigations not indicated unless symptoms persist beyond 4 – 6 weeks

Yellow Flags

- = Barriers to recovery
- Problems at home or work

Management of Back Pain

- Conservative:
 - 80 – 90% of back pain resolves in 4 – 6 weeks
 - Firm bed (eg a board underneath)
 - No slouching, education on how not to stress back
 - Analgesia (→ break cycle of muscle spasm)
 - No bed rest, early return to work
 - Warmth, analgesics
 - Promote self care and responsibility → ↓dependence
 - Stay active. Eg swimming. But may need to modify normal activities. Lift carefully, wear low heeled shoes, chair which helps good posture, pillow between knees at night, walking, cycling, swimming
 - Exercises only help with symptoms – don't affect recovery time
 - Physio – but not while acutely sore
 - Manipulation may help in the first month
 - Advice on prevention
 - Check-ups at 1, 4 and 6 weeks (ACC guidelines)
 - If not improved after 2 weeks, consider X-ray, referral, etc
- Other treatment:
 - Sciatic pain: epidural steroid injection
 - Surgery: remove disc protrusion, decompression or stabilisation

Pelvic Injury

- Serious
- Need to check all midline structures: rectum, bladder, urethra, also ureters, iliac vessels
- Immediate risk is bleeding. Usually from iliac veins – retroperitoneal
- Signs and symptoms of pelvic bleeding:
 - Shock (blood loss, visceral damage)
 - Bruising
 - Abrasions
 - Ecchymoses into thigh and perineum
 - Swelling of labia / scrotum, blood at urethral meatus
 - Abdominal tenderness
 - Pain
- Investigations
 - X-rays essential: AP, inlet, outlet, oblique views. Always look for pairs of fractures
 - If anterior fracture then must also do x-rays of sacro-iliac joints and lumbar

Fractures

- Structure and stability:
 - The stability of the pelvic ring depends on both the bony and ligamentous structures
 - The anterior position of the pelvic ring does not participate in normal weight bearing, nor is it essential for maintenance of pelvic stability
 - The posterior arch (sacrum, sacro iliac joint and ilia) all serve as the weight bearing portion of the pelvis
 - The posteriosuperior SI ligaments connecting the iliac tuberosities to the sacrum provide most of the stability to the SI joints
 - Fractures may be unstable or stable (those that don't involve the pelvic ring or have minimal displacement of the pelvic ring)
- Types of fractures:
 - AP compression injury hinges the pelvis open onto the intact posteriosuperior S.I. ligaments. Not grossly unstable
 - Lateral compression. Caused by direct force to iliac crests. May be stable or unstable
 - Vertical shear. Forces through femur directed perpendicularly to the pelvic ring. Causes disruption to the S.I. joint / unimpacted fracture through the sacrum or ilium. Hemipelvis is unstable
 - If >1 fracture then pelvic ring is unstable and up to 25% will have internal injuries.
- Treatment
 - Quick manoeuvre to ↓ bleeding: internally rotate femurs and tie a towel around the pelvis and pull it tight
 - Most fractures are stable and can be treated conservatively
 - If unstable will require surgical stabilisation

Upper Limb

Shoulder

Exam

- Look:
 - Compare both sides
 - Effusions not seen unless significant.
 - Look at each muscle group
 - If shoulder dislocated, there will be a convexity or flattening of the deltoid below the acromion
- Feel:
 - For tenderness and swelling
 - Start at sterno-clavicular joint → AC joint and corocoid process → gleno-humeral joint → spine of scapula
 - Feel along groove between acromion process and head of the humerus for ligaments of teres minor, infraspinatus and supraspinatus
 - Feel and look in axilla: lymph nodes, check soft tissues for swelling/tenderness
- Move:
 - If active movement is reduced, try passive movement for the remainder of the normal range
 - Abduction: test with elbow flexed. Test passively from behind. Normal is 90°
 - Elevation: If done actively, possible to 180°. Thumbs facing forwards, arms straight. Look for painful arch from 60 – 120° due to insertion of inflamed rotator tendons catching on the acromion. Is it the same with the arm laterally or medially rotated? Checks for tendon impingement
 - Adduction to 50° across the front of the chest. Pain in full adduction if AC joint injury
 - External rotation: with elbow flexed to 90°, can externally rotate to ~ 60°. Good test of glenohumeral joint (eg for frozen shoulder)
 - Internal rotation: Test actively: place hand behind back and scratch as high as they can. Compare with good arm
 - Extension is possible to 65°
 - Testing Rotator Cuff:
 - Pain worst at 90° abduction
 - Supraspinatus: test abduction against resistance, especially from 0 - 30° (deltoid doesn't help much in that range) with thumbs pointing to the ground (turns the glenoid tubercle forward → greater impingement)

- Infraspinatus: externally rotate against resistance
- Subscapularis: ‘Lift-off test’: Hold hand behind back, with patient pushing out from their back. Try and push them in (Pectoralis Major inactive in this position)
- Teres Minor: hard to test in isolation
- Check for stability:
 - Sulcus test: pull arm down and look for sulcus deep to the deltoid muscle (distracting the gleno-humeral joint)
 - Anterior draw test: from the side, hold acromion and corocoid process between your thumb and index finger, hold proximal humerus between the other thumb and forefinger and try and push forward and backwards against each other
 - Apprehension test for dislocating shoulder: posterior pressure during elevation on an abducted and externally rotated arm
 - Push-ups against the wall: look for winging of scapula → seratus anterior dysfunction
- Always examine neck and elbow (joint above and joint below) and distal pulses
- X-rays:
 - Do AP and lateral obliquely – as scapular is oblique and don’t want spine and other shoulder in the lateral film
 - Can do an axillary film: abducted 90% and x-rayed from above
- Differentiating:
 - Intra-articular disease → painful limitation of movement in all directions
 - Tendonitis → painful limitation of movement in one plane only
 - Tendon rupture and neurological lesions → painless weakness
 - Referred pain:
 - Cervical root lesions (eg due to cervical spine lesions)
 - Brachial plexus, thoracic outlet syndromes
 - Referred pain from abdominal visera, diaphragm

Injury

- Most frequently affected by non-arthritis conditions involving bursa and surrounding tendons: tendonitis, bursitis, frozen shoulder
- **Frozen shoulder:**
 - = Adhesive Capsulitis
 - Gradual onset of pain, pain at night, then ↑stiffness as pain gradually subsides
 - May follow minor trauma
 - ↓ Active and passive movement in all directions, following minor trauma. Cause unknown – but due to a tendonitis/capsulitis → adhesion of capsule to the humeral head
 - Treatment: physio, mobilisation, NSAIDs, corticosteroid injection into subarcromial bursa
 - Prognosis: resolution may take years
 - Differential:
 - Disuse stiffness
 - Complex Regional Pain Syndrome Type 1
- **Rotator Cuff:**
 - Humeral head is held in place by the rotator cuff muscles forming part of the joint capsule: infraspinatus posteriorly, supraspinatus superiorly, teres minor and subscapularis anteriorly
 - Due to impingement of rotator cuff tendons under the coraco-acromial arch. May be due to osteophytes or narrowing under the coraco-acromial arch
 - With age or injury the tendons of these muscles are prone to hyaline degeneration, fibrosis and calcification → friction, swelling and pain. Prone to rupture
 - Tendonitis of more than one tendon ⇒ rotator cuff syndrome
 - Presentation:
 - Local tenderness over rotator cuff insertion
 - Supraspinatus tendonitis: the most common: pain on abduction of the arm
 - Subscapularis tendonitis: pain on internal rotation
 - Infraspinatus tendonitis: pain on external rotation
 - May be accompanied by bicep tendonitis: pain on resisted *forearm* flexion and supination and on pressure on the tendon of biceps in the bicep groove
 - Treatment:
 - Conservative:
 - NSAIDs

- Local injection of steroid with local anaesthetic to tendon insertion
 - Rest shoulder initially, in sling if necessary
 - Short-wave diathermy, ultrasound therapy to reduce pain
 - Exercise to lessen the risk of adhesive capsulitis or help restore movement
 - Surgical:
 - ‘Decompress’ the rotator cuff
 - Excise the coraco-acromial ligament, anterior acromial process or any obstructive masses
 - Cuff reconstruction for large tears
- **Anterior dislocation:**
 - Head of humerus anterior to the glenoid fossa:
 - Usually sub-glenoid (ie also inferiorly displaced)
 - Can rarely be subclavicular
 - Mechanism: arm abducted and externally rotated then hit from behind (eg tackle injury)
 - Clinical: Very painful. Patient holds arm at elbow to prevent any movement. Palpate under acromion, is humeral head there?
 - Consequential injuries
 - Check axillary nerve (cutaneous sensation from axillary nerve palsy over regimental badge area [over deltoid on upper arm] and action of teres major – medial rotator and adductor - and deltoid – adduction)
 - Hill-Sacks lesion: injury to posterior of head of humerus
 - Bankart Lesion: injury to the anterior margin of the glenoid fossa
 - Reduction: Kocher or Hippocratic manoeuvres
 - Management: immobilisation in a sling for 2 to 3 weeks while structures anterior to gleno-humeral joint heal (otherwise recurrence), then physio avoiding external rotation
- Posterior dislocation:
 - Mechanism: Direct trauma from the front, electric shocks or Grand mal seizures
 - Head of humerus lies posterior to glenoid.
 - Clinical: Pain, deformity, local tenderness
- Shoulder Instability: 2 types:
 - Atraumatic, multidirectional (ie generalised laxity), bilateral, treatment: rehab (Physio)
 - Traumatic, unidirectional/unilateral, Bankart Lesion (capsule at the front detaches from the glenoid), Treatment: surgery. Progressively less traumatic force required to dislocate it. External rotation causes apprehension
- Fracture of Clavicle:
 - Mechanism: fall on outstretched hand
 - Clinical: arm clasped to chest to prevent movement, subcutaneous lump
 - Xray: usually middle third
 - Treatment: support arm in sling until pain subsides (2-3 weeks)
- A/C Joint:
 - Mechanism: usually involves fall in which patient rolls on shoulder
 - Clinical: Outer end of clavicle prominent, local tenderness present. Confirm subluxation by supporting elbow and detecting movement of clavicle downwards.
 - Clavicle is usually attached to the acromion by the ac joint, coroid ligament and trapezoid ligament. In serious injuries all three of these areas can be damaged
 - Treatment: Broad arm sling for 4-6 weeks usually sufficient
- Infantile Torticollis: Two types
 - Congenital shortening of sterno-mastoid muscle
 - Neurological: damage to the spinal accessory nerve from infected lymph nodes in the posterior triangle
- Brachial Plexus injury:
 - Erb’s Palsy: C5, C6: paralysis of deltoid, supraspinatus, teres major, biceps → Porter’s tip position
 - Klumpke’s Paralysis: C8, T1: arm in adduction, paralysis of small muscles of the hand. May also be Horner’s syndrome

Upper Arm and Elbow

Exam

- In the elbow, look for:
 - Joint effusion

- Lumps: rheumatoid nodules, gouty tophi, enlarge olecranon bursa
- Feel: especially for tenderness over the lateral epicondyle (tennis elbow) or medial epicondyle (golfer's elbow)
- Move: Normal range is from 0° – 150°. Limitation of extension ⇒ early synovitis
- Radiology of elbow:
 - If looking for effusion on an x-ray (eg blood in joint following fracture of the head of the radius) look for protrusion of the Haversian fat pads in the coronoid and olecranon fossa → radiolucent triangles
 - Avulsion of the medial epicondyle in children: 'Little leaguers' injury from pitching in baseball
 - Medial = Trochlear articulates with the ulnar (literally = 'pulley')
 - Lateral = Capitalum articulates with the radius

Injury

- Fracture of proximal humerus:
 - Mechanism: Fall on outstretched arm, most common in post menopausal women
 - Clinical: Appearance of large bruise on upper arm. Signs of axillary nerve or brachial plexus injury should be sought. Exclude dislocation of the shoulder
 - Treatment: Sling. Begin mobilising early as pain permits: gentle arm swinging, climbing fingers up the wall. If > 2 parts fractured, then surgery
 - Major complication: shoulder stiffness
- Humeral shaft fractures:
 - Most treated conservatively – u-slab, collar and cuff, sling, brace, etc.
 - Complication: risk of radial nerve injury in spiral groove
- Supra-condylar fracture of the humerus:
 - Eg child falling onto outstretched hand.
 - Radial pulse may not return for 24 hours
 - Can lead to Volkmann's Ischaemic Contracture due to disruption to the brachial artery. Muscle necrosis (especially FPL and FDP) → flexion deformity at elbow and wrist. Arm is blue, there is no radial pulse and passive finger extension is painful (the key sign)
 - Cast in < 90° flexion
- Fractured Head of Radius:
 - Mechanism: fall on outstretched hand forces elbow into valgus. Common in adults
 - Clinical: Painful rotation of forearm, tender on lateral side of elbow
 - Treatment: Sling
- Fractures of Olecranon:
 - Mechanism: Direct blow or fall on elbow causes a comminuted fracture. Clean transverse break is due to traction when patient falls on hand whilst triceps contracted (attaches to olecranon)
 - Clinical: Graze or bruise over elbow. With a transverse fracture there may be a palpable gap and they are unable to extend elbow against resistance
 - Treatment: Undisplaced transverse needs immobilisation in cast at 60 degrees flexion for 2-3 weeks then exercises begin
- Pulled Elbow:
 - Mechanism: Radial head stretching annular ligament and slipping out from under its cover. Usually kids 2 – 6 years old when parents have pulled on child's arm (esp when crossing road)
 - Clinical: Tenderness over lateral aspect, supination limited
 - Treatment: Sling, usually results in spontaneous reduction
- Tennis Elbow: enthesitis of the common extensor origin on the lateral epicondyle of the humerus → pain on contraction/stretching of the forearm extensors. Management: rest, physio, NSAIDs in the early stages, steroid injections, surgery later on
- Golfer's Elbow (or any throwing sport): Enthesitis of the common flexor origin on the medial epicondyle
- Ulnar Nerve Entrapment:
 - Fracture at elbow or prolonged or recurrent pressure on the ulnar nerve → compression of the nerve in the cubital tunnel
 - Presentation: wasting of the ulnar innervated muscles (hypothenar eminence and the interossei) with sensory loss in the little and ulnar side of 4th fingers
 - Treatment: Decompression
 - NB: Deep motor branch of the ulnar in the hand can be damaged by recurrent pressure from tools (screw-drivers, handlebars, crutches, etc)

Forearm and Hand

Exam

- Naming:
 - Don't number fingers, name them: thumb, index, middle, ring and little
 - Don't describe structures as medial or lateral, use radial and ulnar
 - Palmar surface of hand = volar
- Always examine whole hand and compare with other hand
- Inspection:
 - Work from wrist to finger tips
 - Fingers: ulnar deviation, palmar subluxation, joint swelling
 - Nails:
 - Psoriasis: pitting (small depressions in the nails), onycholysis (white across distal, lateral or proximal portion), hyperkeratosis (thickening of the nail), transverse nail ridges ('tide marks' – signs of previous inflammation)
 - Splinter haemorrhages in rheumatoid arthritis and SLE
 - Rheumatoid vasculitis: small, periungual brown spots
 - Periungual telangiectases in SLE, erythematosus and scleroderma
- Palpation and passive movement together: tenderness, swelling, osteophytes, laxity
- Function:
 - Grip strength: squeeze two fingers. Squeeze a partly inflated sphygmomanometer
 - Key grip: try and pull thumb and forefinger apart
 - Opposition: try and pull thumb and little finger apart
 - Functional test: undo a button, write with a pen
- Testing nerves:
 - Want to test intrinsic muscles that have no extrinsic help
 - Ulnar Nerve (Medial cord, C8, T1)
 - Abductor of little finger
 - Adductor pollicis: grip paper between thumb and side of index finger and try and pull it away. If they bend the thumb, they're trying to use flexors to help (ie fail the test)
 - Lumbricals: flex MCP and extend IP joints. Ulnar does ring and little finger
 - Ulnar claw hand: hyperextend the fingers and the ring and little fingers curve forward due to lack of lumbricals
 - Median Nerve (Lateral and Median Cords, C6,7,8,T1):
 - Opposition of thumb to little finger: requires median eminence. NB opposition of the thumb requires flexion, abduction and rotation
 - Abduction of thumb: Abductor pollicis brevis and longus (other two muscles of thenar eminence can be ulnar)
 - Anterior Interosseous Nerve Compression: compressed under the fibrous origin of flexor digitorum → weakness of FPL, pronator quadratus and flexor profundus to the index and middle fingers → 'Benediction Hand' when they try and make a fist.
 - Radial Nerve (posterior cord, C5,6,7,8):
 - Check back of first web space (between thumb and index finger). Only sensory area reliably supplied by radial nerve
 - Motor distribution:
 - Upper arm: triceps
 - Proximal to supinator, this branch innervates ECRL, ECRB, brachioradialis, supinator
 - Distal to supinator tunnel: EI, ECU, APL, EPL, EPB
 - Posterior Interosseous nerve compression: passing through supinator muscle. Weakness of the long finger extensors, short and long thumb extensors but no sensory loss.
 - Sensory distribution: Terminal part supplies the dorsum of the hand. Posterior Cutaneous branch supplies a variable area on the back of the arm and forearm
 - Common sites affected: axilla (eg pressure from crutches), midhumeral fracture, at and below the elbow (dislocations and Monteggia fractures)
- Testing ligaments:
 - Ligaments: test like knee. Opening to the sides, forward and posterior displacement when fully flexed and then when not quite fully flexed
 - Of flexor pollicis longus: hold proximal phalanx of thumb and flex the end

- Of flexor digitorum profundus: hold middle phalanx and flex distal phalanx
- Of flexor digitorum superficialis: hold other fingers in full extension, hold proximal phalanx of middle finger, flex finger and distal phalanx should be floppy
- Of extensor pollicis longus: can rupture after a Colles fracture → can't straighten distal thumb (Mallet Thumb)
- Napier's ligament: anterior over the 1st CMC joint

Injuries

- Fractures of Radius and Ulna:
 - Mechanism: occur commonly in road accidents, direct blow causes transverse at same level. Twisting may cause spiral or oblique fractures at different levels
 - Clinical: Fracture usually obvious. Pulse must be felt and hand examined for circulatory or neural defects.
 - Treatment: Kids only need cast for 6-8 weeks. Adults often require internal fixation.
 - Fractures of either the radius or ulna alone, with shortening (ie angulation or displacement) are associated with dislocation of the other:
 - *Monteggia Fracture:*
 - Fracture to ulna and dislocation of radial head
 - Mechanism: fall on hand, body twisting at time of impact
 - Clinical: Ulnar deformity obvious, but dislocation may be masked by swelling. Look for pain and swelling on lateral side of elbow. Wrist and hand must be examined for signs of injury to radial nerve
 - Treatment: Restore length to ulna then reduce. Above elbow cast, arm at 90 degrees flexion 6 weeks
 - *Galeazzi Fracture:*
 - Fractured radius and subluxation or dislocation of distal radio-ulnar joint
 - Clinical: more common than Monteggia, important to check for ulnar nerve injury
 - Treatment: As for Monteggia
 - *Colles' Fracture:*
 - Fracture of the radius within 2.5cm of the wrist with dorsal angulation/displacement. If displacement occurs the classic dinner fork deformity occurs.
 - Mechanism: Most common fracture resulting from a fall on the outstretched hand. Sometimes TFCC (Triangular Fibrocartilage Complex) is torn therefore disrupting the distal R-U joint and causing ulnar angulation also
 - Clinical: Pain and tenderness over distal end of radius after a fall. Deformity and radiology also often definitive
 - Treatment: If displaced then reduce, plaster cast in ulnar deviation and slight flexion for 5-6 weeks with finger and wrist exercises
 - Complications: Radial drift or ulna prominence in mal union. Delayed rupture of tendon of extensor pollicis longus due to roughness at site of injury or decreased blood supply (→ Mallet thumb). Carpal tunnel syndrome also possible
 - Smith's Fracture: Due to fall on the back of hand. Reverse of Colles fracture (ie volar displacement rather than dorsal)
 - Barton's Fracture: Intra-articular fracture of the distal radius. Unstable
 - Distal Radio-ulnar joint:
 - Triangular ligament (TFCC): holds radius in place while it rotates around the ulnar
 - Test for dislocation: grip around the proximal wrist and squeeze or supinate → pain
 - *Scaphoid fractures:*
 - Rare in skeletally immature children
 - 2nd in occurrence to radial fracture – usually young adult males
 - Waist of scaphoid the most common site
 - Caused by fall on radial side of outstretched hand → land on tubercle of the scaphoid with wrist hyper-extension
 - Blood supply is distal to proximal pole ⇒ prone to avascular necrosis or poor healing
 - If suspected treat as a fracture, immobilise joints above and below (i.e. Colles cast, with thumb free, up to 10 weeks to healing) – may not see it on first Xray and prone to non-union. Can see on bone scan after about 1 day. However, over diagnosed.

- Carpal dislocations:
 - Perilunate dislocation: associated with distal radius fracture. Lunate stays attached to radius, all other carpal bones pushed dorsally
 - Trans-scaphoid perilunate dislocation: as for perilunate dislocation, but fracture through the waist of the scaphoid leaves the proximal fragment in place. Treatment: reduction/surgery
- Metacarpal Fractures:
 - 5th most common. Treatment: Buddy strapping, or strapping + slab
 - 1st metacarpal: Bennett's Fracture – through middle of the metacarpal and intra-articular through the 1st CMC joint. Following a fall or blow on a clenched fist or forced abduction of the thumb (skiers). Ligament of Napiers can commonly be injured as well. Unstable as oblique and proximal fragment is attached to trapezium and distal fragment has strong muscles attached to it that pull it proximally. Reduce and plaster with thumb held abducted and extended. Transverse fracture is straightforward: Scaphoid cast
 - Multiple metacarpal fractures: twisting and crush injuries. Realignment with Kirschner wires or small bone plate
- MCP dislocation. Uncommon. May require open reduction
- Finger injuries:
 - Mallet Finger: can't extend DIP: rupture or avulsion of extensor tendon, eg by ball hitting outstretched finger. If < one month since injury then splint in extension otherwise surgery (but may not get full flexion back)
 - Button Hole (Boutonniere) Deformity: can't extend PIP joint of finger and hyperextension of DIP: Rupture/detachment of central slip of extensor tendon with lateral bands slipping down the side of the finger
 - Trigger Finger (Stenosing Tenosynovitis): flexor tendon inflames and then jams going through the A1 annular pulley over the MP joint (under the palmar crease). May find crepitus, swelling, triggering and tenderness. Common in RA. Treatment: cut the A1 pulley
 - De Quervain's Syndrome. Pain over the styloid process of the radius (dorsal wrist). Finkelstein's sign: pain on forcible adduction and flexion of the thumb into the palm. Stenosing tenosynovitis/inflamed tendon sheath of extensor pollicis brevis and abductor pollicis longus. Management: Rest, NSAIDs, cortisone injection, surgery
 - Skiers/Gamekeeper's Thumb: rupture of the ulnar collateral ligament of the MCP joint of the thumb, caused by forced abduction. If stable then splint. If unstable (can't oppose fingers) then repair (adductor tendon may get in the way and prevent reattachment)
 - Dislocation of the phalanges: usually always ligament injury as well. Swelling may take up to 2 years to reduce. Reduction can be spontaneous or via longitudinal traction. Buddy strapping + early mobilisation
 - Phalangeal fractures: Buddy taping: encourage flexion, deny rotation, allow for swelling (ie not too tight)
- Dupuytren's Contracture: Painless fibrosis of the palmar aponeurosis (can also occur on the foot). Usually familial (associations with alcoholism and manual work over-rated), anti-epileptics. Causes puckering of the skin over the distal palmar crease and gradual flexion of the fingers (usually starts with ring finger). Treatment conservative. If they can't push their palmer MCP joints into the table then consider surgical release. Prognosis worse if younger
- Ganglia: Painless, jelly filled swelling caused by a partial tear or bulging of a joint capsule. Commonly in the wrist. May resolve or cause little trouble. Don't respond to injection. Surgical excision.

Carpal Tunnel Syndrome

- Compression of the median nerve as it passes through the carpal tunnel in the wrist
- Epidemiology: Common. Usually women 3 - 50 years
- Causes: Due to thickened tendons or synovitis in the carpal tunnel
 - Rheumatoid arthritis
 - Hypothyroidism
 - Acromegaly
 - Pregnancy (2nd trimester to oedema)
 - Obesity
 - Amyloid
 - Diabetes Mellitus
 - Idiopathic
- Symptoms: Pain/tingling in the hand and wrist classically in the median nerve distribution (palm and thumb, index and middle fingers). Wakes at night, shakes hand, can't get it comfortable

- Signs:
 - Wasting of thenar eminence, weak thumb abduction and opposition (late signs).
 - Tinel's Test: pain is reproduced by tapping a tendon hammer over the carpal tunnel
 - Flex both wrists for 30 seconds – may precipitate paraesthesia if carpal tunnel syndrome: Phalen's Test
- Investigations: median nerve conduction velocity test
- Treatment:
 - Light splint to hold wrist in slight dorsiflexion, NSAIDs and vitamin B6
 - Diuretics
 - Corticosteroid injection
 - Surgical Decompression

Lower Limb

Gait

Components of Gait

- Aim of gait is to keep the body's centre of gravity travelling in smooth line → ↓energy
- Gait consists of a:
 - Stance phase (60% of the cycle):
 - Heel strike: Forefoot not yet in contact. Knee in full extension. Quads contract to prevent buckling of the knee
 - Foot Flat: Dorsiflexors slowly relax to bring foot to ground, and hip extensors propel body forward
 - Mid stand: body directly over ankle
 - Heel off: Triceps surae contract
 - Toe off: Hallucis and flexor digitorum longus contract
 - Swing phase (40% of the cycle):
 - Acceleration: iliopsoas contracts (flexes hip), passive knee extension, dorsiflexors contract so foot clears the ground
 - Mid swing
 - Deceleration: hamstrings stop hyper-extension of the knee and gluteus maximus slows hip flexion
 - Double stance: both feet on ground for 20% of the cycle when walking. When running this % reduces to 0% (ie swing > 50% of cycle so both feet off the ground at some point)

Abnormalities of Gait

- Causes a limp
- The main causes of abnormal gait are:
 - Pain → *Antalgic gait* (non-specific). Pain → shortened stance phase on affected leg, shortened swing of opposite leg
 - Weakness
 - Joint abnormality
- Usually noticed during stance phase when one leg is bearing the body's weight
- Swing phase:
 - Abnormal heel strike due to:
 - Pain in hind foot (so land on forefoot)
 - Quad weakness: Knee won't extend by itself, so lands flexed and at risk of buckling. Use hand to push thigh posteriorly (foot and hip fixed so backward pressure on distal thigh stops the knee collapsing). May also land on mid foot
 - Foot Slap Gait: during foot flat phase: weakness of dorsiflexors → foot slaps to the ground rather than controlled lowering
 - Mid-stance:
 - Back-knee Gait: due to:
 - Fixed plantar-flexion deformity of the ankle: Can't dorsiflex ankle above neutral so compensate with knee hyper-extension of the knee (slight flexion is normal)
 - Quad weakness: Use hyperextension of the knee to lock the leg straight, rather than quads holding the knee in extension

- ↓Abductor muscle action: Either weakness (disuse, polio, L5 lesion) or because use puts ↑ pressure across the hip joint → pain if hip pathology:
 - Abductor Lurch or Gluteus Medius Gait: Lateral shift of the trunk over the sore hip in stance, rather than use abductors
 - Trendelenburg Gait: Other hip sags excessively due to inability of abductors to keep pelvis level. Look at hip and shoulder alignment
- Extensor Lurch or Gluteus Maximus Gait: Don't have enough strength in gluteus maximus to hold hip in extension → risk that the torso collapses forward at the end of stance. Lurch torso backwards to compensate
- Flat Foot or Calcanal Gait: can't toe-off, instead lift whole foot off without extending big toe.
Due to:
 - Pain or Rigidity in the fore foot
 - Weakness of plantar-flexors
- Swing Phase:
 - Paralysis of foot and ankle dorsiflexors can cause one or more of the following during toe clearance:
 - Steppage or Drop Foot Gait: flex knee more in swing phase so the foot clears the floor
 - Hip-hike Gait: Lift pelvis to help the foot clear the ground. Can also be due to a stiff knee
 - Circumduction Gait: Swing leg out to the side so the foot clears the ground. Can also be due to a stiff knee
 - Abnormal pelvic rotation: Weakness of hip flexors on the swing side → ↓ acceleration. Compensate with ↑forward pelvic rotation to 'flick' the swing leg forward
 - Hip Fusion: fused hip on the stance side → ↓ pelvic rotation on the swing side → decreased swing length
- Abnormal gaits by causative muscles:
 - Quads: Abnormal heel strike, back-knee gait
 - Abductors: Abductor lurch/Gluteus medius or Trendelenburg gait
 - Gluteus Maximus: Extensor lurch
 - Plantar flexors: Flat foot/calcanal gait
 - Dorsiflexors: foot slap, steppage/drop foot, hip-hike or circumduction gait
 - Iliopsoas: abnormal pelvic rotation
- Other:
 - Broad based gait: impaired balance/co-ordination/vision, drunk
 - Short leg: have to drop ipsilateral hip in stance phase so the foot can reach the floor

Observing Gait

- Walk the patient
- Other aspects of gait to observe:
 - When observing gait, focus on the pelvis first:
 - Pelvic tilt
 - Pelvic rotation
 - Lateral shift of the torso
 - Width of base: normally 6 – 8 cm
 - Stride length (distance from where the heel strikes on one side to where the heel strikes again on that *same side*)
 - Step length (distance from where the heel strikes on one side to where the heel strikes on the opposite side. Normally the same for both sides)
 - Also observe shoulder movement
- Once you've identified the gait, think of causes from top down:
 - Stroke
 - Spinal chord lesion
 - Nerve root
 - Peripheral nerve
 - Muscle (either weakness or pathology)
 - Joint
 - Bone (eg fracture)

Hip and Femur

Overview

- Primary concerns:
 - Range of motion
 - Gait
- Also need to examine
 - The lower back and sacro-iliac joints
 - Vasculation of the leg: pulses, temperature, capillary refill
 - Peripheral nerves: eg sensory
- Problems arising with the hip:
 - Fracture
 - Arthritis
 - Dislocation: trauma, also in congenital abnormalities, infection, Cerebral Palsy
 - Epiphyseal dislocation (typically a chubby 11 year old boy with a slipped femoral epiphysis)
 - Infection: septic arthritis

History

- Impact on daily activities
- Walking distance
- Climbing stairs
- Getting out of low chairs
- Location:
 - Anterior/groin pain: ?hip
 - Lateral: ?trochanteric bursitis, referred from spine
 - Posterior: referred from spine, gluteus medius tendonitis

Hip Exam

- Inspection
 - While standing:
 - Observe gait
 - Walking: on toes (tests S1), on heels (test L5)
 - Observe from front and do Trendelenberg's test: thumb on each ASIS while they alternate standing on one leg. Sagging to contra-lateral side is Trendelenburg positive (ie lack sufficient abductor strength to stabilise pelvis)
 - Observe from back: wasting of gluteals, posterior surgical scars, etc
 - Test the joint above (sacro-iliac joints and lumbar spine): Bend over (measure how far they do down – eg fingers to floor, toes, mid-calf, etc). Extend back
 - Test the joint below: crouch down to test knees
 - Palpate sacro-iliac joints and lumbar spine for tenderness
 - On bed, look especially for:
 - Scars, hernia, bruising, inflammation
 - Muscle wasting: gluteals, quads, biceps and adductors
 - Leg length (check they're lying straight and pelvis is straight):
 - Real leg length discrepancy: Measure ASIS to medial malleolus on each side. If there is a discrepancy then flex both knees to isolate the discrepancy to above or below the knee
 - Apparent leg length discrepancy: measure umbilicus to medial malleolus. If discrepancy but no real leg length discrepancy then postural cause
- Palpation:
 - Groin: lumps: hernias, lymph nodes, femoral artery aneurysm \Rightarrow pain is not hip pain
 - Check for ilio-tibial band pain over the greater trochanter \Rightarrow pain is not hip pain
- Range of motion: always state start and end: from X to Y degrees (eg adduction from 0 to 30 degrees)
 - Compare sides
 - Thomas test for fixed flexion deformity (ie not full extension): Bring up good leg with hand under the spine. When pelvis starts to flex the bad leg won't be able to remain straight if there is fixed flexion deformity. Quantify by measuring the degrees that the bad leg has risen from lying flat
 - Test flexion
 - To test adduction (0 - 20°) and abduction (0 - 50°), stabilise hip by holding hand across both ASIS or abduction the opposite leg

- Internal (0 - 45°) and external rotation (0 - 45°): flex hip and knee and lever hip using lower leg
- Don't test extension
- Finally check:
 - Leg pulses → relevant to operative risks
 - Joint above: did this while standing
 - Joint below: check knee
- X-ray

Injury

- Fracture of Femoral Neck:
 - Commonest site in elderly, associated with osteoporosis
 - Types: subcapital, transcervical, basicervical, intertrochanteric
 - Clinical: History of fall, pain in hip. Patient lies with limb in lateral rotation and leg looks short
 - Location: key issue is disruption of blood flow to the femoral head. Most blood flow is via the attachment of the capsule. If disrupted (via a fracture at or above a basicervical fracture) → avascular necrosis
 - Treatment: Operative mostly. Displaced fractures will not unite without internal fixation. Richardson's screw often used, otherwise hip replacement
 - Complications include: dementia, pressure sores, pneumonia, urinary infection, *not* liver failure
 - Clinical difference between a dislocated femur and a fractured neck of femur: both are shortened. Neck of femur: leg externally rotated, dislocation: leg internally rotated ('in points out and out point in')
- Femoral shaft Fracture:
 - Clinical: Mostly young adults. Shock is severe and with closed fracture fat embolism common. Leg is rotated externally may be short and deformed. Thigh swollen and bruised. Shock MUST be treated, ABG should also be done
 - Risk of fat embolism: do CXR (?pleural effusion, congested pulmonary veins etc)
 - Treatment: Intramedullary nailing
- Comminuted fractures of the femur:
 - Mechanism: violent trauma (eg motor bike accident)
 - Traction or external fixation +/- grafting to fill the gaps
- Supracondylar fracture of the distal femur:
 - Mechanism: Forceful flexion/hyperextension in osteoporotic bone
 - Gastrocnemius then pulls the femur forward
 - Internally fixate with long blade plate
- Condylar fracture of the femur:
 - Mechanism: Fractures entering the intercondylar notch can divide a condyle from the femur (eg knee hitting the dash board)
 - Management:
 - Undisplaced: aspirate + traction for 4 weeks then cast
 - Displaced: open reduction and internal fixation
 - Complications: avascular necrosis, collapse, varus or valgus deformity

Knee

History

- About the injury
 - How did you do it: Direct blow or indirect (eg twisting → consider meniscus lesion)
 - Immediate disability: Inability to walk, knee collapsing (?ACL injury), locking (?meniscus), catching, clicking. For days or weeks, hamstring spasm protects the painful knee. As pain and effusion settle, the knee gradually straightens. NB neither cartilage or inner two thirds of menisci are innervated – pain from these injuries is caused by consequential tension/damage to other structures
 - Sounds and sensations: hearing or feeling a pop, snap or tearing
 - Swelling: If the knee swells straight after an injury → ?ACL injury causing bleeding into the joint or other haemarthrosis (always serious). Soft tissue swelling/effusion takes up to a day
- Always ask about knees:
 - Locking: question carefully to distinguish from pain-induced hamstring spasm
 - Giving way

- Swelling
 - Function:
 - Difficulty with stairs (going up or down?)
 - Trouble getting out of low chairs
 - Waking with pain at night after having leg bent
- Exam*
- **Adequately expose the leg**
 - **Walk:**
 - Stiff knee gait
 - Valgus deviation (deviation away from midline, eg knock knee – Genu valgus)
 - Varus deviation (deviation towards midline, eg bow leg – Genu varum)
 - Lateral thrust: Posterolateral insufficiency, knee goes posterolaterally, a result of Medial Compartment OA.
 - Squat on their haunches and duck walk:
 - Stimulates pain in the front then it is an anterior problem (ie patello-femoral joint)
 - In the popliteal fossa → could be a medial meniscal tear.
 - View from the side: any fixed flexion deformity
 - Inspect the popliteal fossa (then you don't have to get them to roll over on the bed). Look for Baker's cyst – protrusion of the synovium into the popliteal fossa
 - **Look:** Get on bed
 - Swelling
 - Muscle wasting: measure thigh circumference
 - Bony deformity
 - Arthroscopy scars
 - Get them to push their knee down into the bed to test:
 - Extension (fixed flexion deformity)
 - For muscle wasting in vastus medialis
 - Can measure angles with a goniometer
 - **Feel:**
 - Feel for temperature compared with rest of leg and with other knee
 - Feel for effusion (Meniscal pathology often produces an effusion)
 - Stroke/bulge test
 - Patellar tap
 - Palpate joint line along tibial plateau (*watch their face*): Tenderness here may indicate a meniscal tear, above or below the joint line the meniscus won't be causing it.
 - Palpate medial and lateral collateral ligaments
 - Palpate tibial tuberosity and infra-patellar ligament
 - **Move:**
 - Actively raise their leg straight as high as they can: checks extensor mechanism – quads, patella ligament, etc. If damaged traumatically then *urgent surgery* (the key knee injury where you wouldn't wait for the swelling to go down before operating)
 - Flex their knee. Bring the other leg up with the knee in flexion to compare. Have one hand on the patella to feel for crepitus. Measure distance from heel to buttock
 - **Posterior Cruciate Ligament:**
 - Feet back down on the bed leaving both their knees in 90° flexion.
 - Look across the two knees for posterior sag, which could indicate a PCL rupture.
 - Stabilise the tibia (sit on their foot), relax hamstrings and push tibia towards body (Posterior draw test)
 - **Anterior Cruciate Ligament:**
 - Anterior draw to test the ACL. Compare with the other side. Sit on foot and pull tibia towards you
 - Lachman's Test: with leg in slight flexion on the bed (eg rolled up towel or your knee underneath it) push down on distal femur while pulling up on proximal tibia
 - Pivot Test (hard to elicit unless relaxed or under GA): Flex the knee, put it in valgus, then extend it. If ACL is ruptures, the knee jumps smartly forward
 - McMurray's Test for **meniscal tears** (not particularly reliable): Feel and listen for a click as meniscal tag snaps free
 - Start with leg in slight flexion

- Medial lemniscus: externally rotate the tibia on the femur, apply valgus pressure. Extending the leg will cause pain/clicking
- Lateral lemniscus: internally rotate the tibia on the femur, apply varus pressure. Further flexing the leg will cause pain/clicking
- Collateral Ligaments:
 - With leg under your arm Valgus stress test and Varus stress test:
 - With the knee still in 15° steady it as you pull the leg into valgus, this tests the medial collateral ligament and the ACL. Now Push it into Varus, this tests the lateral collateral ligament
 - Lay the leg flat and repeat with the knee in full extension: tests all structures – not just the collateral ligaments. If laxity in full extension, the ACL or PCL damage as well
- **Patellar-femoral joint:**
 - Ask about pain going up and down stairs
 - Palpate
 - Border
 - Anterior surface: Push it in – ‘any pain?’
 - Tendon and ligament insertions (especially tibial tuberosity)
 - Posterior surface (by pushing it to one side and then the other)
 - Solomon’s test: With leg in full extension, try and lift patella and get fingers underneath. If can’t then effusion/synovitis
 - Site on edge of bed with legs handing over: Look at the direction that the patellar points in. Have the patient flex and extend at the knee → should follow an inverted J course
 - Grind or Friction Test
 - Straighten the leg with your hand over the patella
 - Will cause painful grating if the central portion of the articular cartilage is damaged
 - Patella apprehension test: Press the patella laterally and hold it slightly subluxed → Watch the person’s face and ask them to flex their knee → If they grimace or show signs of pain then the test is positive and is diagnostic of recurrent patellar subluxation or dislocation.
- **Joint Above and Below. Check the Hip (pain is referred to the knee from there)**
- Check the Ankle and the foot pulses, and distal neurology

Knee Injury

- General principles of ligament injury:
 - Pain + slight joint opening ⇒ good (strain/partial rupture)
 - No pain + big joint opening ⇒ bad (complete rupture)
- Always x-ray adequately. Small bony fragments on x-ray ⇒ soft tissue injury until proven otherwise
- In kids, bone and growth plates are weaker than ligaments
- Meniscal Tears:
 - Variety of types: fragments causing locking, tears on internal or external margins, etc
 - Clinical: Twisting injury, unable to straighten knee, locking (typically bucket handle tears), pain
 - Investigations: Arthroscopy or MRI
 - Management: Excise tears or reattach. Aim is to preserve as much of the meniscus as possible
- Lateral/Medial Collateral Ligament:
 - Most common knee ligament injury
 - Medial is attached to the medial meniscus. Lateral isn’t → less injury. But if it is, consider check for fibular head fracture and common peroneal nerve damage
 - Mechanical: Blow to medial/lateral side of knee pushing the joint into varus/valgus
 - Presentation: Tenderness over ligament (unless complete rupture → no pain), pain worse under varus/valgus stress, effusion
 - Management: Isolated tears heal well without operating. Immobilisation in leg plaster at 10° flexion (6 weeks) then mobilise cautiously. May have ongoing instability
- Anterior Cruciate Ligament:
 - Prevents posterior displacement of the femur on the tibia and hyperextension. Is the weaker of the 2 cruciates. Anterior-medial bundle is taut throughout flexion → anterior draw test +ive if AMB affected
 - 75% of haemarthroses
 - Mechanism: sharp twisting movement or tackle that pushes the tibia forward cf femur
 - Presentation: may hear a snap, swelling, pain, effusion (very rapid if due to haemarthrosis). If delayed then knee gives way, can run in a straight line but can’t turn corners

- Often tear medial meniscus (\rightarrow OA and instability)
- X-ray for avulsion fracture of tibial insertion: seen in young patients
- Management:
 - Conservative: aspirate and physio to strengthen hamstrings
 - Surgical: reconstruction of ligament (repair impossible as ligaments devitalise rapidly after injury)
- Posterior Cruciate Ligament:
 - Prevents anterior displacement of femur on tibia and hyper-flexion
 - Mechanism: blow to anterior tibia when knee flexed (eg bicycle vs car) or hyperextension
 - Presentation: swelling, pain, effusion, posterior sag at 90° flexion
 - X-ray for an avulsion fracture (\rightarrow requires surgery)
 - Most do well with conservative treatment. Can often manage without a PCL. Quads exercises decrease backwards tibial sag
- Patella Fractures:
 - Comminuted: from blow to flexed knee (eg knee against dashboard). Put patella together (usually hard) or remove it (patellaectomy)
 - Stellate: blow to patella that cracks but doesn't displace fragments. Aspirate + long leg cast
 - Transverse: Due to sudden contraction of quads. Internal fixation with tension wire band
- Chondromalacia Patellae: young women. Patellar aching after prolonged sitting due to softening or fibrillation of the patellar articular cartilage. Conservative treatment: vastus medialis strengthening
- Disruption of extensor mechanism:
 - Rupture of Rectus Femoris: sudden violent contraction \rightarrow transverse tear. Feel defect in muscle. Conservative treatment: ice, elevation, analgesia, mobilisation within limits of comfort. Functional deficit negligible
 - Ruptured Quadriceps tendon: sudden violent contraction. Need to reattach
 - Ruptured patella tendon: Forced flexion injury. Repair if weakness or extensor lag
 - Dislocation of the Patella:
 - Sharp twisting motion on flexed knee or blow to side of leg \rightarrow haemarthrosis (\rightarrow swelling) and medial tenderness (medial structures torn).
 - To reduce: gently extend the knee, then gentle traction. Primary concern is distal circulation \rightarrow reduce at scene of injury if possible
 - Aspirate and irrigate if necessary, splint for 4 weeks
 - Physio to strengthen quads (necessary for patella stability)
 - If recurrent then ?underdevelopment of lateral femoral condyle
- Osteochondral Fractures:
 - In young person, twisting or direct blow can \rightarrow detachment of sliver of bone and cartilage. Most common with patellar dislocation
 - \rightarrow Haemarthrosis and fat from cancellous bone causing a fat-fluid line on lateral radiograph
 - If small then remove, if large then reattach
- Chondral separations or flaps: Fragments of articular cartilage. Need arthroscopy or MRI. Flaps are usually ground away. Separations are removed
- Osteochondritis Dissecans:
 - \downarrow Blood to subchondral bone (cause unknown) \rightarrow focal necrosis of cartilage and bone \rightarrow loose fragment
 - Presentation: pain in young adulthood, worse on walking and hyperextension, M>F, intermittent swelling, maybe locking
 - X-ray: small irregularities on medial condyle +/- fragments
 - Treatment: wait, or surgery if no radiological signs of union
- Bursitis: 16 bursae around the knee. Most commonly affected are:
 - Prepatellar bursa: 'housemaid's knee'
 - Infrapatellar bursa: 'Vicar's knee' – they kneel more upright
 - Anserine bursae: on medial side of the head of the tibia, under the ligaments of semi-tendonosis, gracilis and sartorius
 - Aspiration distinguishes friction bursitis from infective or inflammatory bursitis
- Haemarthrosis of the knee is the most common presenting complaint of a 0% F VIII haemophilia

Management of knee injury

- \downarrow Weight
- Exercises to strengthen hamstrings and quads (eg straight leg raise while seated)

- Check for flattened arches → exercises
- Aquajogging
- Analgesics (NSAIDs, consider COX2)
- If tense haemarthrosis then aspiration will give immediate relief and aid diagnosis (ie send it to the lab: ?blood, infection or gout)

Lower Leg and Foot

Exam

- Look: swelling, deformity, muscle wasting. Deformities include:
 - Hallux valgus: lateral deviation of the MTP joint of the big toe (bunion). Causes: biomechanical, pointed shoes or wearing heals, flat foot (flattening of the longitudinal arch)
 - Hammer toe: Extended at the MTP joint, hyperflexed at the PIP joint, extended at the DIP joint (cf boutonniere deformity of the finger)
 - Claw toes: fixed flexion deformity: extended at MTP joints, and flexed at PIP *and* DIP joints. Due to imbalance of extensors and flexors (eg previous polio)
 - Crowding of the toes: rheumatoid arthritis
 - Sausage deformity of the toes: psoriasis, ankylosing spondylitis and Reiter's disease
 - Inspect transverse and longitudinal arch:
 - Pes Planus: Flat feet. May be valgus and eversion deformity. Normal when a child is learning to walk. If the arch forms when walking on toes then OK
 - Pes cavus: Accentuated longitudinal arches: idiopathic, spina bifida or previous polio → ↑weight on head of metatarsals → pain.
 - Calluses over the metatarsal heads on the plantar surface occur with subluxation of these joints
- Feel and move:
 - Swelling around the lateral and medial malleoli (don't confuse with pitting oedema)
 - Hold midfoot and test dorsiflexion (normal ~ 20°) and plantar flexion (~ 50°)
 - Subtalar joint: test inversion and eversion. Look for tenderness more than range of movement
 - Midtarsal (midfoot) joints allow rotation when hindfoot fixed
 - Squeeze MTP joints: tenderness common in early rheumatoid arthritis
 - Very tender first MTP joint ⇒ ?gout
 - IP joints typically affected in sero-negative arthritis
 - Palpate Achilles tendon for nodules and Achilles tendonitis
 - Palpate inferior heel for plantar fasciitis (can occur with seronegative-arthropathies)

Lower Leg and Foot Injury

- Ankle anatomy:
 - Lateral malleolus of the fibula is firmly attached to tibia by the anterior and posterior inferior tibio-fibular ligaments
 - Talus is held in place by deltoid ligament on medial side and calcaneo-fibular ligament on lateral side
 - Commonest ankle injury occurs when the talus is rotated, fracturing one or both malleoli and rupturing the ligaments
- Fracture of the Tibia
 - Most common site of open fractures
 - Clinical: Skin may be undamaged or obviously divided. Foot rolled outwards, leg bruised and swollen. Need to assess circulation and sensation in toes
 - Treatment:
 - Closed fractures need to be observed for compartment syndrome and soft tissue damage. Obtain fracture alignment and start weight bearing early
 - Open fractures require immediate antibiotics, debridement, then stabilization and rehab
- Distal fibial fracture:
 - Check even, clear joint space around the ankle
 - Check ankle joint is not subluxed
 - Check ligaments on the other side (eg Deltoid). If damaged ⇒ unstable
 - Classified as A, B, C1 or C2
 - If stable, cast for symptomatic relief for 6 weeks
- Diastasis:
 - = Dislocation where no true joint exists

- Separation of the distal tibia and fibula. Talus goes with the fibula. Leads to incongruity of the tibial-talus joint
- Ruptured deltoid: always exclude proximal fibular fracture (Maisonneuve Fracture)
- Dislocation of the ankle: reduce urgently (ie before lengthy transport) otherwise ischaemia of overlying skin
- Achilles Tendon Rupture:
 - Mechanism: Forced dorsiflexion against resistance (eg jumping, due to a forward lunge in squash) – an eccentric injury
 - Presentation:
 - Lie on stomach with foot over end of the bed. Foot normally slightly plantar-flexed. If rupture → neutral position
 - Swelling plus defect felt in tendon. Squeezing is positive (Simmond's test). Foot doesn't move when calf is squeezed
 - Management: Hold the ends together until healed – either surgical or conservative.
 - Conservative: Casting for both: 4 weeks in full flexion below the knee cast then a further 3 weeks with foot half way to neutral. Walking with heeled shoe for a further 8 weeks but not bare-foot. Physio + ultrasound to reduce swelling. Rerupture rate 20%
 - Operative:
 - Makes the tendon heal at the right length, doesn't heal any faster
 - Indicated if: a re-rupture, late presentation (> 48 hours), open wound, or if strong healing necessary (eg athlete)
 - Risk: poor skin healing
 - Nothing vigorous for 6 months post injury
- Ruptured plantaris: severe pain, unable to bear weight
- March Fractures: in the shaft of the 2nd and 3rd metatarsals, following excessive walking. X-rays may be normal. Conservative treatment unless severe, in which case cast
- Lisfranc Dislocation of the 1st TMT joint – may impair blood supply to the medial foot
- Metatarsalgia: caused by:
 - Freiberg's infarction: collapse and reformation of the epiphyses of the 2nd and 3rd metatarsal heads
 - Neuroma of the digital nerve
 - Synovitis
 - Sesamoid fracture
 - Injury
 - Pes cavus

Facial Fractures

Nasal Fracture

- Fracture of the nasal cartilages and nasal bone are common and leave a deformity if not correctly treated
- If a nasal fracture is suspected, hold the patient's nose gently and move it slightly. Pain or abnormal movement indicates a fracture
- Treatment: Dislocated or displaced fractures of the nasal bones need to be repositioned accurately. Refer to ENT

Zygoma

- Fractured by a direct blow to the face.
- If there is bruise over the cheekbone, check zygoma fracture
- On inspection and palpation, the zygoma bone should be depressed
- If untreated, depression zygoma will cause diplopia and damage to the infraorbital nerve.
- Treatment: Fragments need repositioning. May require fixation with wires or external fixation

Orbital Fractures

- If direct trauma to the orbit or eye, look for orbital fracture
- Diplopia and the abnormal position of the eye should lead to the diagnosis
- Treatment: Surgery

Maxilla

- Le Fort classification of maxillary fractures:
 - 1: through the maxilla, leaving nose and orbits intact
 - 2: through the maxilla, into the orbit and across the nose leaving the lateral side of the face mobile
 - 3: same as 2 but fracture extends through the lateral wall of the orbit and across the nose
- All maxillary fractures are an emergency because the lateral wall of the face may be unstable and can fall backwards to obstruct the airway.
- Treatment: Secure airway. External fixation to the skull

Mandible

- Dislocation of the TMJ can follow direct or indirect trauma, or even a wide yawn
- Dislocation can usually be reduced easily if the mandible is intact
- Can recognise a fracture by tenderness when the mandible is palpated or squeezed gently, and by a deranged dental occlusion
- X – ray if in doubt
- Soft tissue swelling round a fractured mandible can obstruct the airway
- Treatment: Surgery. May require internal fixation, interdental wiring and dental treatment

Joint and Bone Infections

Septic Arthritis

- Presentation: systemic illness with fever, usually one joint (knee most common), swelling, effusion, warmth, markedly reduced movement of the affected joint, and very painful to move (cf adjacent osteomyelitis → some pain only). Hip and shoulder have less swelling
- In neonates, may overlap with acute haematogenous osteomyelitis
- Risk factors: diabetes, recurrent steroid injections, systemic steroids, alcoholic liver disease, immunosuppression
- Differential:
 - Gout and pseudogout
 - Haemarthrosis
 - Acute osteomyelitis
 - Acute traumatic arthritis
- Pathogenesis:
 - From haematogenous spread or extension of osteomyelitis, often following distant infection. Also following penetrating injury
 - WBC enzymes rapidly erode articular cartilage → surgical emergency: empiric antibiotics and rapid drainage. Urgent – can destroy a joint in 24 hours. In neonates/kids can damage growth plate → growth disturbance
 - S. Aureus, also S pneumoniae and S pyogenes. In high-risk groups, M Tb and Candida. Neonates consider S agalactiae, Haemophilus and N gonorrhoea (did they have bacterial conjunctivitis soon after birth?). Pseudomonas from foot wound.
 - Tb arthritis: usually haematogenous spread from lungs to hips (kids), knees (adults) or spine. X-ray shows marginal erosions and destruction of sub-chondral bone (like Rheumatoid – but different distribution). Have granulomas (except in AIDS). Histology: Granulomas are pink, cf lymphoid aggregates in Rheumatoid that are blue
- Investigations:
 - *Joint aspiration* (arthrocentesis: opaque fluid with WBC > 50,000/ml)
 - FBC, ESR, CRP, **blood cultures**, plain Xray, US (for detection effusion)
 - Xray delays rather than establishes the diagnosis
- Management:
 - Flucloxacillin: for staph aureus, but also covers S pneumonia, S pyogenes, S agalactiae
 - If neonate:
 - And unimmunised consider H. Influenzae: cefuroxime or cefotaxime
 - Consider G –ive: gentamycin
 - Arthroscopic washout
 - Initial splinting for pain relief, but then encourage mobility
 - If there is a joint prosthesis, revision may be necessary

- Complications due to delayed diagnosis:
 - Joint degeneration, joint dislocation
 - Damage to the growth plate → growth arrest

Osteomyelitis

- Common in low socio-economic and warmer weather
- May follow minor trauma with or without infection elsewhere in body
- Acute haematogenous osteomyelitis:
 - Presentation:
 - Early: short, febrile illness, bone pain, metaphyseal tenderness (point tenderness)
 - Late: Swelling/erythema (suggest abscess). Cellulitis. Adjacent joints sore but some movement still possible
 - Vascular supply to bone is compromised and infection spreads to surrounding soft tissue
 - Differential diagnosis:
 - Septic arthritis
 - Cellulitis
 - Trauma (Fracture)
 - Tumour
 - Aetiology:
 - Trauma/surgery → direct introduction of bacteria
 - Direct extension from infective site: eg dental infection → jaw, diabetic foot → bones of foot
 - Haematogenous seeding:
 - Commonest site in children is metaphysis of the long bones. Femur and tibia account for >½ all cases (especially around knee joint). Epiphyseal growth plate acts as a barrier to the spread of infection to the joint. May spread through Haversian and Volkmann's canal system to form a subperiosteal abscess (requires drainage)
 - In adults, haematological spread less common. Tends to affect subperiosteal cortices of long bones. Also cancellous bone of vertebral bodies, may → compression fracture
 - Eg: sluggish blood flow → easy thrombosis following trauma → predisposes to infection (esp staph aureus)
 - Pathology: Inflammatory response → oedema → compromise vascular supply → necrosis → spread of infection through cortices → pus under periosteum → shearing of periosteum → further disruption to blood vessels
 - Causative organisms:
 - Under one year: staph aureus, strep agalactiae, E coli. May be non-specific illness
 - Children: staph aureus, strep pyogenes, H influenzae
 - Adults: staph aureus, staph epidermidis and G negatives (E coli, salmonella and pseudomonas from foot wounds)
 - M. Tb and Candida in high risk groups
 - Complications:
 - Spread of infection → septicaemia, joint infection
 - Fracture, abscess formation
 - → Chronic osteomyelitis in 5 – 20% of cases
- Subacute osteomyelitis: Focal rather than systemic response to infection. Xray shows bone destruction. Differential includes bone tumour and stress fracture
- Chronic osteomyelitis:
 - Usually delayed or inadequate treatment.
 - Pain, swelling +/- discharging sinuses.
 - Xray: destruction, with sequestrum (areas of necrotic bone which can't be resorbed) harbouring bacteria and involucrum (formed from periosteum raised over an abscess). Brodie's abscess: abscess surrounded by sclerotic bone due to organisms of low virulence
 - Treatment: sequestrum must be removed, may require repeated surgery. Poor penetration of antibiotics
 - Complications:
 - Persistently discharging sinus
 - Chronic ill health
 - Pathological fractures/deformities
 - Malignant change → SCC

- Investigations:
 - Blood: FBC, ESR, CRP, Blood cultures (+ive in 50%)
 - Imaging:
 - Plain films: no changes until day 10
 - US: subperiosteal abscesses
 - Bone scan: very sensitive but not specific
 - MRI: very sensitive but expensive
 - CT: good for detecting degree of bone destruction
- Treatment:
 - High dose IV antibiotics for at least 2 – 4 days (for children, Flucloxacillin 50 mg/kg/6 hourly, max 2 g), followed by 3 – 4 weeks of oral therapy
 - Surgery to decompress and remove necrotic bone if late or failed medical treatment, or subperiosteal abscess drainage
- Specific presentations:
 - Osteomyelitis of the calcaneum: infection 5 – 10 days after puncture wound. *P aeruginosa*
 - Discitis: inflammation of the lumbar disc, usually < 8 years
 - Pelvic osteomyelitis: pain referred to the abdomen, buttock or leg. *S aureus*. Bone scan diagnostic
 - Tb Osteomyelitis: rare in developed world. Occurs in 1-3% of patients with pulmonary Tb. Insidious. After months: pain on movement, fever, night sweats, weight loss. Destructive. If lumbar or thoracic vertebrae may → hunchback deformity

Pyogenic infections of the hand

- Usually history of trauma
- Paronychia: common infection of periungual tissues, usually by *Staph Aureus*
- Felon: deep infection of the pad of the finger. Usually *Staph aureus* following puncture wound
- Cellulitis: Strep Pyogenes infection
- Suppurative flexor tenosynovitis:
 - Infection of flexor tendon sheaths
 - Presentation: Swollen finger with painful motion. Symmetrical swelling, tenderness, erythema along tendon sheath. Semi flexed posture and severe pain on passive extension of DIP joint
 - Signs: crepitus, erythema, vesicle formation, colour, pain, puss
 - Tests:
 - Culture of puss, blood culture, FBC
 - X-ray to rule out foreign body, air in tissue or joint, associated fracture
 - Treatment: irrigate, leave wound open and dress after swelling has decreased, antibiotics, splint
- Atypical infections:
 - Herpes infections of the thumb and fingers (eg Whitlow's lesions)
 - Fungal infections: more indolent. Sporotrichosis common

Metabolic Bone Disease

- Osteoporosis: bone matrix reduced in amount but normally mineralised (ie ↓bone mass due to loss of both protein matrix and Ca in equal proportions)
- Osteomalacia: normal amount of bone matrix but deficient mineralisation (ie ↓Ca)
- Both will appear on x-ray as osteopenia (poverty of bone)

Bone Metabolism

- Osteoblasts:
 - Synthesise osteoid: normally this is a thin layer as the time between matrix deposition and mineralisation is short. If either ↑osteoid or delayed mineralisation → thick layer (hyperosteoidosis), eg:
 - ↑Bone formation: fracture callus, Paget's disease, hyperparathyroidism
 - ↓Calcium, phosphorous, or vitamin D
 - Blocked mineralisation due to inhibitory/toxic substances (eg aluminium, iron, fluoride)
 - Mediate osteoclast activity
 - Flat when inactive, plump when active. Become buried in cortex (then called osteocytes)
 - ↑Activity due to physical activity, ↑PTH, growth factors, fluoride. Suppressed by inactivity and steroid hormones

- Osteoclasts:
 - Regulated by PTH and osteoblasts
 - Large cells containing 2 – 4 nuclei
 - Adhere to bone and are seen in depressions referred to as Howship's lacunae or resorption bays → scalloped appearance of resorbed bone
- Woven bone: immature bone laid down by osteoblasts in a callus (eg healing of a fracture)
- Lamellar bone: parallel and organised
- Tetracycline:
 - Give pulses before bone biopsy
 - Binds to actively mineralising surfaces and fluoresces in UV light under the microscope
 - Shows the extent of mineralisation and amount of bone formed over a given time

Osteoporosis

- Normal bone composition – just less of it. Either primary or secondary
- Epidemiology:
 - Often presents with a hip fracture. 3 per 1000 in men and 6 per 1000 in women over 65 per year.
Number of vertebral fractures and resulting disability unknown
 - $\frac{1}{4}$ of those > 80 going to hospital with a fracture don't return to their previous residential status
- Pathogenesis:
 - Bone is constantly turning over. From the 3rd decade, resorption exceeds bone formation – the two become uncoupled. In women, this accelerates post menopause (oestrogen is protective). Around menopause will lose 6 – 10% of bone mass, then returns to gradual decline
 - Trabecular bone (20% of skeleton) turnover 8 times that of cortical bone (80% of skeleton). Femoral head has lots of trabecular bone ⇒ good place to measure loss. Use Singh Index of number of trabecular groups present (6 = good, 1 = bad)
 - Also thinning and attenuation of the cortices
 - Fracture risk a combination of density (which we can measure) and structure (which we can't)
 - By the time they present with a fracture, osteoporosis is usually advanced
- Severity depends on:
 - Peak bone mass. Peaks at around age 30. Largely determined by type of inherited vitamin D receptor. Also calcium intake in teens, etc
 - Sex: peak bone mass of males > females
 - Age: men affected later than women
 - Also physical activity positive (disuse → localised osteoporosis), smoking negative, calcium intake
- Distribution:
 - Osteoporotic vertebrae (most common fracture):
 - Loose secondary trabeculae 1st (leaves vertical lines of primary trabeculae) → clear glass appearance
 - Changes in shape: wedge, biconcave, planar (ie flat)
 - Anterior of vertebrae reduced
 - May occur with trivial trauma or lifting
 - Small fractures don't cause immediate pain – comes on after several days. If no scoliosis then can heal
 - Fractures affecting proximal femur, proximal humerus, distal radius resulting from falls
 - Look for insufficiency factors in the sacrum, pubis, and supra acetabular
- Differential of osteoporosis:
 - Male: hypogonadism (→ ↓testosterone), excess alcohol
 - Female: ↓Ca and Vit D post menopause
- Scanning for osteoporosis:
 - Plain x-ray insensitive: don't show changes until 30 – 40% of bone mass lost. Radiodensity varies due to exposure, developing, and patient's build
 - Dual Energy X-ray Absorbiometry = DEXA:
 - Measures bone density (ie Ca density) by firing X-rays of 2 different wave lengths – one maximally absorbed, the other absorbed as much as carbon, and subtract the two
 - Number of standard deviations from the mean (of 30 year old women) more important than actual density. $T < -2.5$ standard deviations = Osteoporosis. Osteopenia: $-1 < t < -2.5$
- Management:
 - Prevention:
 - Physical exercise (→ ↑bone laid down)

- Adequate Ca (prevents bone resorption)
- Vitamin D if house bound (a small amount of sun is sufficient)
- Rocaltrol: 1,25(OH)2D3
- HRT: most stop before 5 years – compliance problem. Can start at any age – but if elderly need to build up gradually
- Treatment: alendronate (or Fosamax) → ↓osteoclast action → ↓turnover → gain bone

Osteomalacia

- Osteomalacia in adults = Rickets in kids
- Present with bone pain, fractures (eg neck of femur) or waddling gait (proximal myopathy)
- Aetiology:
 - Deficiency or abnormal metabolism of vitamin D
 - Calcium deficiency
- Pathology:
 - Intracortical tunnelling (due to secondary hyperPTH)
 - Coarsened indistinct trabecular pattern (due to seams of osteoid) → frosted glass appearance
 - Looser's zones: the hallmark of osteomalacia: lateral margin of scapula, ribs, pubic rami, proximal femur, proximal ulna
 - Micro: ↑↑ in unmineralised bone (up to 40 – 50%) + disorganisation of trabecular architecture
- In children: changes around metaphyses of most rapidly growing bones (knee and wrist), with irregular and broadened epiphyseal growth plates
- Investigations:
 - X-rays: generalised osteopenia + multiple, bilateral, symmetrical partial linear fractures (stress fractures)
 - May be ↑ALP, ↓vitamin D
 - PTH assay not very helpful: normal range is too wide (0.5 – 5) so can mask an increase. Mild increase → ↑osteoclastic activity, but serum Ca normal so remineralising normally → osteopenia and not osteomalacia

Increased Bone Resorption

- *Hyperparathyroidism:*
 - See also Parathyroid, page 101
 - Old term: osteitis fibrosa cystica
 - ↑PTH (either primary or secondary) → ↑Ca and ↓PO₄
 - Presentation: kidney stones, peptic ulcer, bone pain, nausea, vomiting, weakness, headaches, depression (bones, stones, groans). Now rare – usually picked up as an incidental finding of hypercalcaemia
 - Affects cortical bone more than cancellous/trabecular bone
 - ↑Osteoclast and osteoblast activity
 - May → reactive fibrosis tissue (eg following microfractures and secondary haemorrhages) → mass called a 'Brown tumour'
 - X-ray: generalised osteopenia and *tufts on end of distal phalanges*
 - Differential:
 - Blood sample with dehydration or tourniquet → ↑Ca
 - Malignant disease and/or neoplastic syndrome with PTHrH secretion
 - Sarcoidosis
 - Vit D intoxication
 - Diuretic therapy
 - Treatment: neck exploration for parathyroid adenoma
- *Renal Osteodystrophy:*
 - = All skeletal changes resulting from chronic renal disease, including:
 - ↑Osteoclast resorption (mimicking hyperPTH)
 - Delayed matrix mineralisation (osteomalacia)
 - Osteosclerosis
 - Growth retardation
 - Osteoporosis
 - Due to:
 - PO₄ retention → Secondary HyperPTH → ↑Osteoclast activity
 - Metabolic acidosis → bone resorption

- ↓ Conversion of 1,25(OH)2D3 in kidneys → hypocalcaemia
- Aluminium deposition (from antacids, dialysis fluid) at the site of mineralisation → ↓mineralisation
- Similar impact to osteomalacia: ↑PTH → osteoclastic bone resorption
- Investigations:
 - X-ray and bone densitometry
 - Bloods: Ca, albumin, phosphate, PTH, ALP, Vitamin D3 levels
 - Urine Ca usually low and faecal Ca high
- *Paget's Disease:*
 - Common in northern Europeans, rare in Blacks/Asians, M = F, usually old
 - Presentation:
 - Monostotic, asymptomatic and incidental finding on x-ray (doesn't spread)
 - In a small number, widespread, polystotic lesions with bone pain (worse at night), fracture, arthritis or development of a sarcoma
 - Usually axial skeleton (spine, skull, pelvis) and femur
 - Pathogenesis: ?viral infection (paramyxovirus) of osteoclasts → ↑↑ osteoclast activity → ↑↑ osteoblast activity → disorganized, woven bone. Normal bone mineralisation. Also genetic and geographic predisposition
 - Gross: enlarged bone with thick cortices
 - Micro: irregular trabeculae with numerous osteoclasts and plump osteoblasts, jigsaw pattern
 - Prognosis:
 - Progressive bone deformity and micro fractures, anterior bowing of the femur. Arthritis due to deformed joints
 - Osteosarcoma in 5 – 10% of those with severe disease
 - Investigations:
 - X-ray: early radiolucency. Late: loss of distinction between cortical and cancellous bone (may be confused with primary bone tumour)
 - ↑Bone formation → ↑↑ALP but Ca and PO4 normal. ↑Urinary hydroxyproline
 - Treatment:
 - Mild: NSAIDs – indicated if pain
 - Severe: bisphosphonates (alendronate), calcitonin
 - Complications:
 - Fractures
 - Spinal stenosis → nerve compression
 - Osteosarcoma
 - Enlargement of the skull, femur, clavicle, tibia ('Sabre Tibia')
 - Neural deafness due to bone overgrowth
 - High output heart failure (due to ↑ blood flow to bone)

Orthopaedic Tumours

- Primary bone tumours are rare.
- Myeloma accounts for half of malignant bone neoplasms:
 - Old, M > F, pathogenic fractures, pepper-pot skull, normocytic anaemia with Rouleaux
 - Gross: red current jelly lesions
 - See Multiple Myeloma, page 302
- Classification based on histology of tumour cell – cell of origin is unknown/debated. Diagnosis difficult. Requires clinician, radiologist, pathologist
- Classification:

Histologic Type	Benign	Malignant
Haematopoietic		<i>Myeloma</i>
Chondrogenic	<i>Osteochondroma</i>	<i>Chondrosarcoma</i>
	<i>Chondroma</i>	Secondary chondrosarcoma
	<i>Chondroblastoma</i>	Mesenchymal Chondrosarcoma
	<i>Chondromyxoid fibroma</i>	
Osteogenic	<i>Osteoid osteoma</i>	<i>Osteosarcoma</i>
	<i>Osteoblastoma</i>	Parosteal osteosarcoma

Unknown	Giant Cell Tumour	Malignancy in giant cell tumour <i>Ewing's sarcoma</i>
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Chondrosarcoma

- Malignant tumour of cartilage, with *no tumour osteoid* or bone being formed
- Pain becomes severe and persistent, swelling
- Typically *age 40 – 60* (average 45 years)
- Most common in the medullary cavity of the flat bones of the pelvis, large limb bones and ribs. Rare to involve the extremities
- Types:
 - Conventional: eg diaphysis or metaphysis of long bones. Margins poorly defined. Eroded or thickened cortex. X-ray: fluffy calcification. Grossly, pearly blue/white colour of cartilage
 - Secondary to multiple exostosis in chondrodysplasia
 - Dedifferentiated
- Treatment: tend to metastasise late (to lung and other bones) → attempt local excision and replacement with prosthesis
- Prognosis: Grade 1 and 2 80 – 90% 5-year survival, Grade 3 (rare) 40% 5-year survival. Local or distant metastasis may occur up to 20 years later

Osteosarcoma (Osteogenic Sarcoma)

- Proliferating malignant spindle-cell stroma *producing osteoid*
- After multiple myeloma, it is the most common primary malignant bone tumour
- 50 – 60% of cases are near the knee (either distal femur or proximal tibia)
- Types:
 - Conventional osteosarcoma: Most common. Adolescent growth (*age 10 – 20*). M:F = 2:1, eg *metaphyses* of distal femur and proximal tibia. X-ray: geographic destruction, dense or lytic, raised periosteum. May also appear fibroblastic or predominantly chondroid. Gross: haemorrhagic. Micro: osteoid formation, malignant spinal cells (often see spindle cells in mesenchymal tumours)
 - Second, smaller peak in 60 – 70s, secondary to existing disease (eg in < 1% of Paget's), previous irradiation, etc. Microscopically look like a osteosarcoma
 - Also Telangiectatic osteosarcoma, low-grade osteosarcoma, small cell osteosarcoma (like Ewing's but produces osteoid) and surface osteosarcomas (on the surface of the bone)
- Investigations: X-ray, serum ALP (markedly ↑), and biopsy
- Very aggressive: assumed to have metastasised at diagnosis – usually to lung (in preference to lymph nodes)
- Treatment: chemotherapy → resection → prosthesis → post-op adjuvant chemo (high dose methotrexate)
- 5 year survival 60%

Other

- Benign:
 - Osteochondroma: most common benign tumour of bone. Growth of an aberrant focus of cartilage on the surface of the bone (?adherent growth plate). Cartilage-capped lateral bony projection from the metaphysis, usually long bones. Also known as an exostosis. Can be hereditary (→ multiple). Symptoms due to size, impingement or fracture. X-ray: mushroom like growth from metaphysis. Regular shape. If irregular then ?malignant
 - Enchondroma: benign cartilaginous neoplasm usually arising in the medullary cavity of bone. Most common in age 20 – 50 in small bones of the hand or foot. Usually clearly circumscribed. Differential is chondrosarcoma – suspect if large bone in an older patient, erosion of the cortex or suspicious histology
 - Chondroblastoma: benign chondroid neoplasm at the end of long bones during teens
 - Osteogenic tumours: produce osteoid:
 - Osteoid osteomas: Rare. Males in teens. Exquisite pain especially at night relieved by aspirin. Well-circumscribed lesion of bony trabeculae, with variable mineralisation. < 1.5 cm. X-ray: radiolucent central zone surrounded by opaque sclerotic bone
 - Osteoblastoma: Roughly speaking, an osteoid osteoma that is > 1.5 cm
 - Fibrous dysplasia: developmental defect of bone formation → enlargement and distortion of the bone. Feels firm, fibrous and may be gritty.

- Malignant:
 - Ewing's Tumour: Rare. t(11;22)(q24;q12) usual → fusion gene is an oncogene. *Usually age 5 – 10*. Usually shaft of long bones, presenting with localised pain or swelling. Small round blue cell tumour. ?neural origin. 75% 5-year survival. Can mimic osteomyelitis
 - Giant Cell Tumour: F > M, age 20 – 40, ends of long bones, lytic lesions, contains multinucleated giant cells. Usually benign. High local recurrence, rarely metastasises
 - Fibrosarcoma
 - Malignant tumour of fibroblasts (ie collagen producing cells)
 - Occurs in any connective tissue but more common in the extremities and middle aged
 - Fibrosarcoma of the bone is rare. Swelling, pain, pathological fracture
 - Synoviosarcoma:
 - Rare malignant tumour of the synovium, usually sharply circumscribed
 - Rapid enlargement of the joint with pain. Usually knee, hip or shoulder
 - May extend along fascial lines and invade bone
 - Treatment: if small then excise, if high grade: resection + radiotherapy + chemotherapy

Secondary Bone Cancer

- Most common bone cancer ⇒ always ask about previous primaries
- Source: breast > prostate > kidney > lung > thyroid
- Sites: vertebrae, pelvis, proximal femur, humerus
- Spread: usually haematogenous. Occasionally local extension
- Usually osteolytic → pathological fractures
- Presentation:
 - Pain + history of cancer in 50 – 70 year old
 - In children < 6 years: from neuroblastoma
 - Symptoms of hypercalcaemia: anorexia, nausea, weakness, depression, polyuria
- Investigations:
 - Xray: usually osteolytic lesions (if osteoblastic probably carcinoma)
 - Bone scan, FBC, ALP, Electrophoresis (myeloma)
 - FNA: determining cell of origin helps guide management
- Treatment: usually palliative, control pain, prophylactic fixation, spinal stabilisation, radiotherapy (↓ pain)

Arthritis Overview

Exam

- Screening exam (OHCS, p 666):
 - Observe from behind: muscle bulk (shoulders, buttocks), straight spine, swellings, deformities
 - Observe from the side: cervical and lumbar lordosis, thoracic kyphosis
 - Touch your toes: spine and hip flexion
 - Observe from in front
 - Ear to shoulder: lateral cervical flexion, flexion, extension and rotation
 - Open and close the mouth: TMJ, orofacial pain
 - Hands behind head: shoulder and sternoclavicular movement, then straight above
 - Arms straight: elbow extension
 - Examine hands: nails, pray sign, press dorsum of both hands together
 - Observe legs: bulk, swelling, deformity
 - Knee effusion
 - Observe feet
 - Observe walking

Differentials for Arthritis

Causes of Monoarthritis

- Acute Monoarthritis:
 - Septic arthritis: either haematogenous (staph or gonococcal) or following penetrating injury
 - Traumatic
 - Gout, pseudogout

- Haemarthrosis (eg haemophilia)
- Sometimes seronegative spondyloarthritis
- Chronic monoarthritis:
 - Chronic infection (eg Tb)
 - Osteoarthritis
 - Seronegative spondyloarthritis
 - Metastasis

Causes of Polyarthritis

- Acute polyarthritis
 - Infection: viral (mumps, rubella, EBV, etc), bacterial
 - Rheumatic fever
 - Onset of chronic polyarthritis
 - Drug allergies
- Chronic polyarthritis:
 - Rheumatoid arthritis
 - Seronegative spondyloarthritis
 - Primary osteoarthritis
 - Gout, pseudogout or hydroxyapatite arthropathy
 - Connective tissue disease (eg SLE)
 - Infection (eg Tb)

Differential by Distribution

- Inflammatory:
 - Peripheral, symmetrical, small joint polyarthritis:
 - RA
 - Lupus and Connective Tissue Diseases (non-deforming and non-nodular)
 - Asymmetrical, large joint, oligoarthritis, possibly with spinal disease: Sero-negative spondyloarthropathies:
 - Ankylosing Spondylitis
 - Reactive Arthritis and Reiter's Disease
 - Psoriatic Arthritis
 - Arthritis of IBD
 - Acute inflammatory mono or oligo arthritis: septic arthritis or gout
- Non-inflammatory:
 - Osteoarthritis: weight bearing joints or hands
 - Soft tissue or locomotor pain syndromes
- Sacro-ilitis: occurs in Ankylosing Spondylitis, Reiter's Syndrome, Crohn's Disease, Chronic Polyarthritis

Causes of Arthritis and Nodules

- Rheumatoid arthritis
- SLE (rare)
- Rheumatic fever (very rare)
- Granulomas, eg sarcoid (very rare)

Raynaud's Syndrome

- Episodic digital ischaemia, precipitated by cold or emotion
- Fingers ache and go pale → blue → red/purple (pain most severe in this stage, during reperfusion)
- May be:
 - Idiopathic: Raynaud's disease
 - Associated with underlying cause (Raynaud's phenomenon): Scleroderma, SLE, RA, arteriosclerosis, leukaemia, drugs, etc. *Not* polyarteritis nodosa
- Keep warm, stop smoking, try Ca channel blockers (eg diltiazem)

Radiology

- Principles: Looking for:
 - Morphologic change in an individual joint
 - The skeletal distribution

- Features:
 - Joint space narrowing, either localised or uniform
 - Erosions (if at the margin then periarthritis erosions)
 - Osteophytes: bony lip at edge of joint
 - Subchondral cysts: formed by synovium getting through fissures in the cartilage
 - Subchondral Sclerosis: micro-fractures in the subchondral bone → attempted repair → dense white band
 - Periarthritis osteopenia: cytokine mediated thinning of the surrounding bone (check other joints)
 - Periarthritis soft tissue swelling:
 - Fusiform: in inflammatory
 - Asymmetric: in gout
- Features of different arthropathies:

	Rheumatoid	Primary Osteoarthritis	Gout
Signs	<ul style="list-style-type: none"> • Uniform joint space narrowing • Erosions • Periarthritis osteopenia • Fusiform soft tissue swelling • Can get cysts (call geodes in RA) 	<ul style="list-style-type: none"> • Localised joint space narrowing (ie not whole joint space) • Subchondral cysts • Marginal osteophytes • Subchondral sclerosis 	<ul style="list-style-type: none"> • Erosions (often paraarticular or long way from the joint, may have cave like opening with overhanging margins) • Relative preservation of joint space and bone density until late in the disease • Asymmetric soft tissue swelling
Distribution	<ul style="list-style-type: none"> • Hand: proximal joints • All large joints • <i>Symmetric</i> 	<ul style="list-style-type: none"> • Weight bearing joints: hip, knee, C5-C6 (fulcrum for flexing the neck) • Distal Hand: DIP, PIP and 1st carpo-metacarpal joint • <i>Asymmetric</i> 	<ul style="list-style-type: none"> • Any small joints of hands and feet • Elbows and knees • <i>Asymmetric</i>

- Other arthropathies are variations on this:
 - Secondary osteoarthritis (eg due to previous trauma or infection). Looks like OA but not standard (eg uniform joint space)
 - If inflammatory but wrong distribution → ?sero-negative
- Idiot's rule of thumb for hand arthritis:
 - Rheumatoid: MCP and MTP joints
 - Psoriasis: PIP joints
 - Osteoarthritis: DIP

Osteoarthritis

- = Loss of articular cartilage in a synovial joint, and associated changes in underlying bone and other joint tissues
- Is degenerative not inflammatory
- Very common, although prevalence unknown due to variations in diagnosis
- Risk factors:
 - Age: 75% of over 70 year olds and 90% of 80 year olds
 - Previous injury
 - Female and obesity (especially hip and knee) are debated
- Non-specific symptoms:
 - **Pain:** initially with/after exercise or at the end of the day, later also at rest and related to other factors. Pain with sleeping on hip at night
 - Stiffness: not as prominent as in inflammatory arthritis
 - Swelling: due to ↑synovial fluid (may contain a few mononucleocytes) and bony thickening
 - Loss of function (common to all arthritis)

- Signs: joint instability, crepitus, joint tenderness, derangement, ↓ range of movement, effusion, fixed deformity
- Distribution:
 - Primary osteoarthritis:
 - Often – but not always - symmetrical
 - Fingers: DIP and PIP, MCP joint of thumb but not of fingers. Can lead to Heberden's Nodes: marginal osteophytes at the base of the distal phalanx. Bouchard's Nodes on proximal IP joints
 - Weight bearing joints: Hips, knees
 - Less Common:
 - Acromioclavicular joints
 - Lower cervical and lumbar spine
 - MTP joints of big toes
 - Secondary Osteoarthritis (secondary to joint disease or injury – consider especially if it doesn't fit the joint distribution of primary):
 - Asymmetrical
 - Trauma (eg intra-articular fracture, dislocation, etc)
 - Infection
 - Metabolic: haemophilia, gout (or pseudogout if bigger joints), haemochromatosis
 - Avascular necrosis: see Complications of Fractures, page 234
 - Congenital (eg DDH)
 - Inflammatory (reactive or primary)
 - Neoplasia (eg prostate → femoral head)
- Pathology:
 - Cartilage = collagen proteoglycans + water (70%). Made by chondrocytes
 - ↓Elasticity of cartilage → mechanical stress causes deformation and stress on underlying bone. Fissuring and flaking of cartilage. Roughened cartilage surface. Blood vessels invade cartilage. ?Inflammatory cytokines mediate cartilage destruction
 - Micro: villus fronds in cartilage
 - Gross: Shiny, subchondral bone (eburnisation), subchondral cysts, osteophytes (extra-articular overgrowth of bone → attempt to ↑ weight bearing area)
- Investigations:
 - X-ray
 - Lab tests usually normal (check for normal ESR, CRP, RF, ANAs, joint aspirate)
- Management:
 - Conservative:
 - Inform, education
 - Do nothing, or
 - Pharmacology (analgesics, NSAIDs): Paracetamol. NSAIDs have little evidence of further improvement, and cause renal impairment and GI bleeds. Potential for COX-2 inhibitors. Also glucosamine (from health food shop, 1500 mg/day)
 - Steroid injection if secondary inflammatory component
 - Physiotherapy:
 - Obtain and maintain full range of motion (↓range of motion → ↑loading on a smaller area of cartilage → wears out faster)
 - Exercise: eg quad exercises for osteoarthritis of the knee
 - Orthotics and other devices:
 - Weight loss and devices to reduce weight bearing across affected joints
 - Raising bed and chairs to reduce strain, walking sticks, handrails, etc
 - Aspiration of joint fluid
 - Surgery, especially for knee and hip (determined on functional/pain criteria):
 - Arthroscopic debridement (buys time)
 - Osteotomy: take out a wedge of bone above or below the joint – realigns stress through the joint → more even wear
 - Arthroplasty: a prosthesis (considerable variety). Main indication is pain. Surgery to correct fixed flexion deformity is less successful. NB don't forget DVT prophylaxis
 - Arthrodesis: joint fusion

Inflammatory Arthritis

Management of Inflammatory Arthritis

- The different arthropathies overlap
- The issue is less which arthritis it is, but whether there are risk factors for serious disease (of which the type of arthritis is but one factor). This risk assessment will determine whether treatment is aimed at:
 - Aggressive treatment: use of immunosuppressives and DMARDs to induce/maintain remission
 - Symptomatic treatment
- Risk factors for any inflammatory disease:
 - Evidence of active inflammation: eg morning stiffness, ↓function, biochemical markers
 - Extra-articular involvement: eg lung, vasculitis, etc
 - Gradual onset (this is worse than sudden onset)
 - Large joint involvement
 - Genetic markers: HLA DR1 and DR4, etc
 - Presence of rheumatoid factor (-ive prognostic factor for erosions in rheumatoid arthritis)
 - Radiographic abnormalities

Blood tests in Inflammatory Arthritis

- Gout and seronegative arthritis are not normally positive for rheumatoid factor and auto-antibodies
- Rheumatoid Factor: IgM against Fc portion of IgG. Can be tested with the Rose-Waaler titre. Positive in:
 - 70-80% of RA
 - < 40% of SLE
 - 100% of Sjogren's
 - 30% of PSS
- ANA: Autonuclear Antigens
 - Screening test of SLE: present in > 95% at titre > 1:200 – but not specific
 - Present in RA (30%), Sjogren's (68%), PSS (64%), and normal (0 – 2%)
 - Also ↑ with age, other autoimmune diseases, drugs, infections
 - Patterns:
 - Diffuse ANA suggests dsDNA may be +ive
 - Speckled ANA suggests ENA may be +ive
 - Anti-DNA histone: suggests active SLE. Also in 95% of drug SLE
 - Anti-centromere: suggests systemic sclerosis
- dsDNA: 70% of SLE. Specific (ssDNA is not). Titres correspond to clinical activity and risk of nephritis
- ENA: Extractable Nuclear Antigens (not all speckled ANA results are due to ENAs):
 - Anti-Ro (SSA): Sjogren's, SLE (30%)
 - Anti-La (SSB): Sjogren's. Always associated with SSA. Found in only 10% of SLE
 - Anti-Sm: 30% of SLE. Specific
 - Anti-RNP: SLE (40%), polymyositis, scleroderma, mixed disorders
 - Anti Jo-1: polymyositis and dermatomyositis
- Anti-phospholipid antibodies (attacks phospholipid on platelets)
 - Occurs in 50% of SLE. Do Lupus anti-coagulopathy test
 - 3 types:
 - Lupus anticoagulant: Causes ↑APTT, but causes thrombosis in vivo
 - Anti-cardiolipin
 - False positive VRDL test
 - 1 and 2 associated with fetal loss, clotting, thrombocytopenia, valvular heart disease
 - Antiphospholipid Syndrome: recurrent miscarriages, thrombocytopenia and recurrent arterial or venous thrombosis
- ANCA: Associated with some small vessel vasculitis. Can divide arteritis into ANCA +ive and -ive (although pANCA may also be found in 20% of polyarteritis nodosa):
 - Cytoplasmic anti-neutrophil cytoplasmic antibody (cANCA): Specific but not sensitive for Wegener's disease > 90% +ive
 - Perinuclear anti-neutrophil cytoplasmic antibody (pANCA): Microscopic polyangiitis ~ 75% (vasculitis in kidney and lung) and PAN
 - ANCA negative small vessel vasculitises include Henoch-Schonlein Purpura

- CD4+:CD8+ ratio (normally ~3) ↑ in Polymyalgia Rheumatica

Pharmacology

NSAIDs

- Action: Many! Inhibit PG synthesis by inhibiting cyclo-oxygenase (converts arachidonic acid to PGG2 and PGH2):
 - COX-1: present in blood vessels, stomach, kidney (eg might actually help in heart disease – eg aspirin)
 - COX-2: induced during inflammation → PGs (eg Celecoxib/Celebrex and rofecoxib/Vioxx)
- Effects:
 - Analgesic: Effective against pain where PGs sensitise nociceptors
 - Anti-inflammatory: Reduce vasodilation, oedema, pain. Effect may not be clinically obvious for 2 – 3 weeks
 - Antipyretic: acts in hypothalamus
- Pharmacokinetics: well absorbed, no first pass metabolism (except aspirin), highly protein bound
- Side effects:
 - ↑ Risk in elderly
 - GI: dyspepsia, mucosal irritation, ulceration (relative risk 5 times, ↑↑ if on warfarin, etc)
 - Renal: Little effect on renal function in normal people. If chronic renal impairment, CHF, gout, or longer T $\frac{1}{2}$ NSAIDs then Na retention and oedema in 3 – 5%
 - Skin: rashes, urticaria, photosensitivity and erythema multiform
 - Other: headache, ↓platelet function → ↑bleeding time, blood dyscrasias (aplastic anaemia with indometacin and phenylbutazone)
- Interactions:
 - ↓Antihypertensive effect of ACE inhibitors
 - ↓Diuretic action of frusemide and thiazide diuretics
 - ↑Methotrexate levels
 - Not if on anti-coagulants → GI bleed
- Patient instructions: Only take them PRN to avoid risk of bleed – so don't take them on good days. Watch for abdominal pain, black stools. Smoking and alcohol ↑ the risk. Don't supplement them with OTC NSAIDs
- Commonly used NSAIDs:
 - Salicylates: Aspirin (not in kids) and Diflunisal
 - Propionic Acids (better tolerated and more sensitive for COX-2): Ibuprofen, Naproxen
 - Pyrazoles: Phenylbutazone
 - Acetic Acids: Indometacin (potent, CNS side effects), sulindac
 - Paracetamol (no anti-inflammatory or GI effects)

Other Pain relief

- Amitriptyline: a TCA which in low dose has pain modifying effects
- Tramadol: opioid analgesic with less respiratory depression, ↓constipation and ↓addiction

Immune Suppressive Drugs

- For acute inflammatory problem (arthritis, connective tissue, etc)
- Prednisone: 60 mg/day starting dose
- Methylprednisolone (iv)

Disease Modifying Anti-Rheumatic Drugs (DMARDs)

- Aim: to suppress inflammatory activity → ↓destructive changes (NSAIDs reduce inflammation but don't act on the pathway that leads to joint destruction)
- Indicated for patients at an early stage with high markers of disease activity ⇒ don't wait for RF, nodules or erosions
- Effect:
 - Suppress inflammatory activity
 - Reduce the need for NSAIDS and corticosteroids which have greater potential toxicity
- First line agents (high efficacy especially in combination, low toxicity):

- Sulphasalazine: start low, increase to 2-3g per day. Best tolerated and most often used. Effect after 3 – 6 months. SE: nausea, rashes, ↓sperm count, hepatitis, oral ulcers, rarely: blood dyscrasias, Stevens-Johnson, neutropenia, monitor CBC and LFTs
- Methotrexate: Takes several months to work. Action: ↓IL-1, ↑IL-10, ↓neutrophil chemotaxis. SE: nausea, bone marrow suppression, GI ulceration, teratogenic. Inhibits folate metabolism → give folic acid 5 – 10 mg/wkly, rare: irreversible liver toxin. Monitor CBC, LFTs, Cr
- Antimalarials: Hydroxychloroquine: weak disease modifying drug, doesn't stop periarticular osteopenia. SE: nausea, rash, headache, tinnitus. Rarely: bone marrow suppression, corneal & retinal damage. Monitor: Cr and 6 – 12 monthly ophthalmological review. Chloroquine more toxic.
- Others:
 - Gold: Sodium Aurothiomalate / Myocrisin. Similar efficacy to Sulphasalazine/methotrexate but more toxic. When it works it works well. Action: accumulates in macrophages. SE: rash, thrombocytopenia, nephrotic syndrome, proteinuria. Not with allopurinol, SLE, breast feeding, liver/renal disease. Monitor CBC, Cr, Urine dipstick for protein
 - Cyclosporin A: SE nephrotoxicity
 - Salazopyrin
 - Beneficial but don't alter progression of radiological changes:
 - Azathioprine
 - D-Penicillamine. SE: ↓marrow, proteinuria, ↓taste, oral ulcers, myasthenia, Goodpasture's
- The future: anticytokine therapy: eg against Tissue Necrosis Factor

Rheumatoid Arthritis

- Persistent, symmetrical, deforming, peripheral arthropathy
- Epidemiology:
 - Peak onset: 4th decade
 - Prevalence: 1-3%
 - Female:male = 3:1
- Pathogenesis:
 - Microbial agent initiates the disease: current suspect is EBV, plus others
 - Presentation of (unknown) antigen to CD4+ T-helper cells + plasma cells and macrophages → cytokine-mediated synovial neutrophilic exudate + ↑vasularity → cartilage-degrading enzymes + fibrosis + panus formation (inflamed synovium) + ↑osteoclastic activity + ligament and tendon damage
 - → Painful, unstable, disrupted joint (eg subluxed, deformed, etc)
 - 65 – 80% are HLA DR4 or DR1 +ive, plus further specific DR alleles (eg Q(k/R)RA motif in the DRB1-HV3 region of the T-cell antigen receptor)
 - Autoimmunity to type 2 collagen can be demonstrated in most patients with RA
 - 80% have Rheumatoid Factors: autoantibodies (mainly IgM) to the Fc portion of autologous IgG
 - Implicated mediators are cytokines: TNF, IL-1, IL-6, IL-15, interferon- α , growth factors, proteases, elastases
- Presentation:
 - Common: Swollen, painful, stiff hands and feet, especially in the morning. Progresses to larger joints
 - Less common:
 - Palindromic: relapsing and remitting monoarthritis of different large joints
 - Persistent monoarthritis (especially the knee)
 - Systemic illness: ↓weight, pericarditis, pleurisy
 - Vague limb girdle aches
 - Sudden-onset widespread arthritis
 - Greatest damage occurs in first 4 – 5 years
- Pattern of involvement:
 - Usually symmetrical
 - Most RA involves:
 - PIP and MCP joints and wrists (DIP spared) in the hands
 - Tarsal and MTP joints in the foot
 - Also involves:
 - Elbows
 - Shoulders (eg Pencilling – erosion of distal end of the clavicle)

- Small joints of upper cervical spine: Atlanto-Axial instability: anterior subluxation of C1 on C2 with cervical flexion due to erosion of the transverse atlantal ligament → threatens spinal cord
- Lumbo-sacral region usually spared
- Hips
- Knees
- Deformities:
 - Initially sausage-shaped fingers and MCP joint swelling
 - Ulnar deviation and volar subluxation (partial dislocation) of the fingers
 - Fingers: Swan Neck and boutonniere (buttonhole)
 - Z deformity of the thumb: hyperextension of the IP joint and fixed flexion and subluxation of the MCP joint
 - Subluxation of the wrist, with prominent radial head
- Extra-articular involvement:
 - Nodules: subcutaneous central zone of fibrinoid necrosis surrounded by palisading histiocytes and fibroblasts. May occur in viscera, including heart, lung and GI
 - Anaemia
 - Lymphadenopathy
 - Vasculitis
 - Carpel Tunnel Syndrome (early manifestation)
 - Multifocal neuropathies (= Mononeuritis Multiplex): Sequential, multifocal, random involvement of non-contiguous peripheral nerve trunks (there are other causes besides RA)
 - Splenomegaly
 - Eyes: episcleritis, scleritis, keratoconjunctivitis sicca
 - Pericarditis
 - Pulmonary fibrosis
 - Amyloidosis
 - *Not* glomerulonephritis
- Investigations
 - X-ray
 - Bloods: Rheumatoid factor +ive in 75% (See Blood tests in Inflammatory Arthritis, page 270)
- Treatment:
 - Regular exercise
 - Physiotherapy
 - Occupational therapy
 - Household and personal aids (eg wrist splints)
 - Intralesional steroids
 - Surgery
 - Drugs:
 - NSAIDs (eg ibuprofen): Least likely to cause a bleed. Contraindicated if asthma or peptic ulcer. To control inflammation/pain
 - Steroids: To control flare-ups. Can reduce erosions if given in early disease. Need to keep dose low (ie 7.5 mg/day) – but due to symptomatic improvement patients often want more. SE: ↓bony density, cataract, fluid retention, peptic ulcers
 - Disease modifying drugs: See Disease Modifying Anti-Rheumatic Drugs (DMARDs), page 271. All have side effects, monitoring essential. All can cause rash

Juvenile Rheumatoid Arthritis

- = Arthritis beginning at or before 16 years of age (usually early childhood)
- = Still's Disease
- Signs: High, swinging, early evening fever, pink maculo-papular rash, arthralgia, arthritis, myalgia, generalised lymphadenopathy
- Number of different types:
 - Oligoarthritis (persistent): asymmetrical, affecting 4 or fewer joints, especially wrist, knees, ankles. Usually remission in 4 – 5 years
 - Oligoarthritis (extended): Oligoarticular onset progressing to > 4 joints
 - Polyarticular JCA: Usually in teenagers progressing to widespread joint destruction, especially hands (less so the DIPs)

- Extra-articular involvement can include: pericarditis, myocarditis, pulmonary fibrosis, glomerulonephritis, uveitis and growth retardation
- Differences from Adult RA:
 - Oligoarthritis is more common
 - Systemic onset is more frequent
 - Large joints affected more than small joints
 - Rheumatoid nodules and rheumatoid factor are usually absent
 - ANAs often positive
- Treatment:
 - Referral to specialist
 - Low dose NSAIDs/paracetamol (Aspirin: beware of Reyes Syndrome)
 - Corticosteroids
- Prognosis: variable: up to 50% have long term disability
- Completely different disease entity to Juvenile Spondyloarthropathies – although clinically may overlap. Enthesitis common

Spondyloarthropathies (Seronegative Arthritis)

- Rheumatoid factor is negative – but exclude seronegative RA
- Clinical overlap between the conditions
- Acronym: PEAR: Psoriasis, Enteropathic, Ankylosing Spondylitis, Reactive/Reiter's
- Have in common:
 - Involvement of spine and sacroiliac joints (= axial arthritis)
 - Usually asymmetrical large joint mono or oligo-arthritis
 - Inflammation then calcification of tendon insertions (enthesopathy)
 - Extra-articular manifestations: uveitis, aortic regurgitation, upper zone pulmonary fibrosis
 - Familial tendency + HLA-B27 +ive predisposition
- If type not clear then classified as 'Undifferentiated spondyl-arthropathy':

	AS	Reiter's	Reactive	Psoriatic	Enteropathic
Sex	<i>M > F</i>	<i>M > F</i>	<i>M = F</i>	<i>F > M</i>	<i>F = M</i>
Age of onset	~ 20	Any	Any	Any	Any
Uveitis	++	++	+	+	+
Conjunctivitis	-	+	+	-	-
Peripheral joints	Lower>Upper	Usually lower	Lower>upper	<i>Upper>lower</i>	Lower>upper
Sacroiliitis	Always	Often	Often	Often	Often
HLA-B27	95%	80%	80%	20 – 50%	50%
Onset	Gradual	<i>Sudden</i>	<i>Sudden</i>	Variable	Gradual
Symmetry spinal	+	-	-	-	+

Ankylosing Spondylitis

- = Chronic systemic inflammatory disorder of the axial skeleton, affecting SI joints and spine
- Ankylosing = fibrous replacement of the joint → bony fusion
- Epidemiology:
 - Prevalence: 2 – 5 per 1,000 males. Men have more progressive disease
 - Men more common and present earlier (6:1 at 16 years, 2:1 at 30 years)
 - Onset usually between 15 – 40 years
 - Closely linked to HLA-B27:
 - 5 – 20% risk for positive individual
 - 11 HLA subtypes identified with different disease susceptibilities
 - Strong ethnic variances in HLA prevalence: present in Caucasians, absent in indigenous people of South America and Australia, high prevalence in Eskimos....
- Clinical presentation:
 - 75% first present with insidious onset of dull back ache, worse at night, improved by exercise
 - Morning stiffness, backache, sacroiliac pain, loss of spinal movement (spinal ankylosis, distraction of < 10 cm on flexion with Schober's test)
 - Leading to flattening of lumbar spine, thoracic kyphosis, neck hyperextension
 - Fatigue common
- Distribution:
 - Sacroiliac joints and spine (lumbar to start with, C-spine later):
 - Bilateral sacro-iliac joint tenderness

- Tenderness of the lumbar vertebrae
- Loss of thoracic kyphosis and lumbar lordosis
- Early restriction in lateral flexion of the spine – test by seeing how far they can slide their hand down the side of their leg without bending forward. Later loss of movement in all directions
- Hips (30%), also knees and shoulders
- Peripheral arthritis infrequent
- Other features:
 - Commonly:
 - Enthesitis
 - Iritis/Anterior Uveitis (25 – 30%): unilateral, acute, painful, with photophobia and blurred vision. To test: shining light in opposite eye causes pain in the affected eye
 - Costocondriasis + chest pain referred from thoracic vertebrae
 - Chest wall rigidity → ↓VC
 - Plantar fasciitis
 - Rare:
 - Neurological involvement: secondary to spinal fracture (eg C-spine), atlanto-axial subluxation, cauda equina syndrome
 - Amyloidosis
 - Carditis and aortic regurgitation due to fibrosis of the aortic valve (can also affect AV bundle → arrhythmias)
 - Apical lung fibrosis (rare)
- Pathogenesis:
 - Cross reactivity between Klebsiella pneumoniae antigens and HLA B27
 - Antibody complexes cause synovitis, enthesopathy (including tendon attachment calcification) → capsular ossification, ankylosis (bony fusion) of the sacroiliac joint, inflammatory arthritis of the synovial joints in the spine and ossification of spinal ligaments
- Diagnosis is clinical: History of inflammatory spine disease + SI tenderness, ↓L-spine mobility, ↓chest expansion
- Differential from RA:
 - Spine rarely affect in RA
 - Small peripheral joints rarely affected in AS
 - In AS there are no subcutaneous nodules and no RF (but there may not be in RA either)
- Investigations:
 - X-rays: ‘bamboo’ or ‘railroad’ spine, squaring of vertebrae, syndesmophytes, erosions of the apophyseal joints (between rib tuberosities and spinal processes), eventually bony ankylosis of the SI joints (also seen in Reiter’s and Crohn’s diseases)
 - Bloods:
 - FBC (mild normochromic anaemia in 15%)
 - ↑ESR and CRP
- Treatment:
 - Physiotherapy/Exercise (not rest) to maintain posture and mobility
 - NSAIDs to relieve pain and stiffness (especially phenylbutazone). If ineffective try sulphasalazine
 - Local corticosteroids for uveitis, enthesitis, peripheral synovitis
 - Disease Modifying drugs if severe

Psoriatic Arthritis

- Epidemiology: occurs in 5 – 7% of psoriasis patients, age 35 – 45, male = female
- Pathology:
 - Can have a reactive type presentation due to a host of possible infective/inflammatory agents
 - Primary lesion = synovitis (similar to RA): hypertrophic villi, T-cell infiltration, aggregates of T cells. But usually only minimal joint impairment. Articular destruction in a subset (25%) with panus formation, cartilage erosion, etc = Arthritis Mutilans
- Clinical presentation:
 - Usually psoriasis develops first, then arthritis, but 15% go the other way
 - Usually insidious but can present acutely
 - Check for nail pitting, transverse ridging, onycholysis
 - Extra-articular manifestations are uncommon (except for conjunctivitis and iritis)

- Distribution:
 - Often asymmetric, mainly oligo but can be poly arthritis
 - Often upper limb
 - DIP joints in hands and feet especially affected – unique to PA
 - Sacroiliac joints and spine (20 – 40%) – asymmetric involvement common
 - Rheumatoid pattern
 - Inflammation of digital tendon sheaths → sausage finger (dactylitis)
 - Enthesitis: Achilles tendonitis and plantar fasciitis
- Diagnosis: Psoriasis (exclude seborrhoeic dermatitis and fungal infections) or psoriatic nail involvement + sero-negative arthritis. Increased likelihood in B27 +ive
- Investigations: X-ray of hands → DIP involvement + resorption of the terminal phalanges
- Treatment:
 - NSAIDs for pain – but may worsen skin lesions
 - Corticosteroid injections for local synovitis
 - If severe: methotrexate, cyclosporin, sulphasalazine, gold etc
- Differentiating from RA:
 - Presence of skin rash
 - Asymmetric
 - DIP and PIP involvement
 - Can overlap with RA and present as a symmetrical, destructive arthritis. Look for psoriasis and nail changes

Reiter's Syndrome

- Classic triad: urethritis, conjunctivitis and seronegative arthritis. Recurrence in 50%, attacks can last several months
- Caused by sterile synovitis following chlamydia/NSU/shigella infection
- Distribution of arthritis usually lower limb (may be chronic or relapsing):
 - Sacroiliac joints and spine
 - Hips
 - Knees
 - Ankles and most of the joints of the feet
- Other features:
 - Iritis
 - Keratoderma blenorrhagica (brown, aseptic abscesses on soles and palms)
 - Mouth ulcers
 - Circinate balanitis (painless serpiginous penile rash)
 - Enthesopathy (plantar fasciitis, Achilles tendonitis)
 - *Not* onycholysis (differentiates from psoriasis)
- Investigations:
 - Chlamydia: First of 2 glass urine test shows more debris in the first glass in urethritis (cf prostatitis where there is more in the 2nd)
 - Anti-chlamydial antibodies
 - Neutrophils in synovial fluid
 - X-rays: periosteitis at ligamentous insertions. Rheumatoid like changes if chronic
- Pathogenesis: following non-specific urethritis, Chlamydia or Shigella infection in those genetically pre-disposed (ie HLA B27). Hyperaemic synovial membrane, but no panus or cartilage erosion (except if progressive). Profuse osteolysis and formation of new periosteal bone
- Management: treat causal agent, rest, NSAIDs, steroid injections, recovery may be slow

Other Reactive Arthritis

- Infective causes: Yersinia, Chlamydia, Campylobacter, Salmonella, Shigella, Clostridium difficile... (all have lipopolysaccharide in their outer cell membrane)
- → Sterile immunological reaction in joints due to cross reactivity of antigens
- Usually B27+
- Presentation:
 - Acute asymmetrical polyarthritis (esp of lower limb) 1-2 weeks post infection lasting for 3 – 6 months
 - Can become chronic with relapsing and remitting course
 - Enthesitis is common (eg → plantar fasciitis or Achilles tendonitis)

- Can also get:
 - Skin lesions resembling psoriasis: Circinate balanitis, keratoderma blenorragica and nail dystrophy
 - Iritis
- Investigations:
 - Causative agent: Blood culture/serology for antibodies/stool culture
 - HLA-B27, X-ray, ESR, joint aspiration for septic arthritis
- Diagnosis is clinical
- Management:
 - Treating persisting infection has little impact on course
 - NSAIDs/corticosteroids
 - Sulphasalazine etc if necessary
- Also in leukaemia, endocarditis, acne, acromegaly, Wilson's disease, sarcoid, sickle cell, haemochromatosis

Enteropathic Arthropathies

- Associations:
 - Inflammatory bowel disease (15% of Crohn's and UC get arthritis)
 - Also associated with intestinal bypass surgery and Whipple's Disease
- Asymmetrical lower limb mono- or oligo arthropathy
- No joint destruction
- Sacroiliitis or Spondylitis in 5% (70% of these have HLA-B27)
- Manage underlying condition:
 - Sulphasalazine for both bowel disease and arthritis
 - NSAIDs and steroid injections for monoarthritis

Crystal Arthropathy

Gouty Arthritis

- Prevalence: ½ - 1%, male:female = 5:1. Common in Maori and Polynesian populations. Most people with hyperuricaemia don't have gout
- Family history common
- Types:
 - Acute Gout:
 - Severe pain, redness and swelling, may be febrile
 - Differential of acute gout: septic arthritis or haemarthrosis
 - Chronic Recurrent Gout:
 - Urate deposits with inflammatory cells surrounding them (tophi) in avascular areas: pinna, infra-patella and Achilles tendons, joints, eye, etc ⇒ chronic tophaceous gout = gouty tophi
 - Bone erosion and loss of cartilage
- Distribution:
 - Acute gouty arthritis is usually monoarticular
 - Affects MTP joint of the great toe in 75% of cases
 - Ankles and knees involved after recurrent attacks
 - Fingers, wrists and elbows affected late
- Pathogenesis:
 - Uric acid is the last step in the breakdown of purines
 - Hyperuricaemia (uric acid > 0.41 mmol/L) → deposition of monosodium urate crystals (MSU) in joints (and viscera, especially the kidney) → chemotactic to leukocytes and activate complement → accumulation of neutrophils and macrophages → erosion, inflammation, secondary OA
 - May be precipitated by trauma, surgery, starvation, infection and diuretics
 - Hyperuricaemia results from ↑ turnover or ↓ excretion
 - Causes of ↓ excretion:
 - Primary gout
 - Renal failure → hyperuricaemia which rarely → gout
 - Hypertension
 - Primary hypoparathyroidism
 - Hypothyroidism

- ↑Lactic acid production (eg from ETOH)
- ↑ Cell turnover (\rightarrow ↑turnover of purines) due to:
 - Lymphoma, leukaemia, severe psoriasis, haemolysis, muscle necrosis
 - Disorders of purine synthesis (eg Lesch-Nyhan syndrome)
- Hyperuricaemia can also cause renal failure eg cytotoxic treatment
- Diagnosis:
 - *Needle shaped, negatively birefringent* urate crystals in tissues and synovial fluid (serum urate not always ↑) – also neutrophils (+ ingested crystals)
 - ↑ESR
 - Check renal function and BP
 - X-rays: in early stages may only show soft tissue swelling
- Treatment:
 - Acute:
 - NSAID (eg ibuprofen, Naproxen, indometacin, not aspirin) – but problematic in renal failure and heart failure (\rightarrow fluid retention). Also contra-indicated if on anticoagulants (\rightarrow GI bleed)
 - Colchicine
 - Prevention:
 - Avoid purine-rich foods (offal, oily fish, beer), ↓ obesity and excess alcohol (which is why it used to be called the ‘disease of kings’)
 - No aspirin: salicylates competes with uric acid for excretion \rightarrow ↑serum urate
 - Long term (‘interval’) treatment: Allopurinol:
 - Xanthine-oxidase inhibitor \rightarrow ↓serum urate
 - But not during an acute attack – wait three weeks. Mobilises gouty tophi \rightarrow ↑systemic urate \rightarrow precipitates acute gout. Use with colchicine cover
 - SE: rash, fever, ↓WCC
 - Allopurinol can also be used during chemotherapy for leukaemia/lymphoma/myeloma to prevent gout from ↑purines
 - Also uricosuric drugs (\rightarrow ↑excretion): probenecid or sulfapyrazone

Pseudogout

- = Calcium Pyrophosphate Deposition (CPPD)
- Onset in 30s
- Deposition of chalky white crystalline material – usually calcium pyrophosphate
- \rightarrow Chondrocalcinosis: deposition in articular cartilage \rightarrow calcification on x-ray
- Predominantly large joints (especially the knees)
- Aspirate: *positively birefringent rhomboid shaped* crystals
- In some there are signs of hyperparathyroidism and haemochromatosis

Connective Tissue Diseases

- = Collagen vascular diseases
- Affect many organ systems, associated with systemic fever and malaise, run a chronic course, respond to steroids, associated with anaemia of chronic disease and a raised ESR

Systemic Lupus Erythematosus

- Non-organ specific autoimmune vasculitis with positive ANAs
- Epidemiology:
 - Peak age of diagnosis: 30 - 40
 - Female:male = 9:1
 - Prevalence: 0.2%
 - Commoner in pregnancy, Afro-Caribbeans, Asians
 - Genetic predisposition: HLA B8, DR3, DR2
- Presentation (OHC p 672):
 - Gradual or sudden onset
 - General: Fever (77%), splenomegaly, lymphadenopathy, extreme fatigue
 - Musculo-skeletal symptoms (95%): joint/muscle pain, non-erosive *small joint* polyarthritis, bone necrosis, rare joint deformity due to capsular laxity

- Skin (81%): photosensitive butterfly rash (hyperkeratosis, follicular plugging), scarring alopecia, Raynaud's, purpura, oral ulcers, discoid lupus (3 stage rash: erythema → pigmented hyperkeratotic oedematous papules → atrophic depressed lesions), nailfold vasculitis
- Renal (<75%): proteinuria, casts, oedema, uraemia, glomerulonephritis. See Systemic Lupus Erythematosus, page 208 for renal complications
- CNS (<18%): Depression, psychosis, fits, cranial nerve lesions, retinal exudates
- Pulmonary (<48%): Pleurisy (+/- effusion), fibrosing alveolitis, BOOP
- CVS (38%): ↑BP, pericarditis, Libman-Sacks endocarditis
- Blood: Normocytic anaemia (75%), Coombs +ive haemolysis, ↓WCC, ↑INR, ↓platelets, ↑ESR, normal CRP
- Mortality is due to renal failure
- Pathology: Autoantibodies → fibrinoid change → fibrosis
- Investigations:
 - FBC
 - ESR > 20, CRP often low
 - 80% are ANA +ive: High dsDNA ANA almost exclusive to SLE (+ive in 40 – 60%)
 - 40% are RF +ive
 - 30% are anti-Sm positive
 - Lupus anti-coagulopathy test
 - Antibodies to Ro (SS-A), La (SS-B) and anti-RNP (ribonuclear protein) help define overlap syndromes
 - VDRL false positive in 30%
 - Organ/skin biopsy
 - Pain disproportionate to radiological damage on X-ray
- Monitoring:
 - BP
 - Urinalysis
 - FBC, U&E, Complement (C3, C4 – better than ESR)
 - dsDNA ANA titres
- Treatment:
 - Sun block creams
 - Analgesics/NSAIDs: joint pain, swelling, fever
 - Hydroxychloroquine for skin and joint pain. For disease not controlled by NSAIDs SE: retinopathy – check eyes annually
 - Prednisolone: higher dose for exacerbations, lower dose for chronic disease – mainstay of treatment
 - Cyclophosphamide: either daily or monthly pulse (fewer side effects): helps renal function more than steroids
 - Azathioprine: steroid sparing. SE: lymphoma
 - Cyclosporin or methotrexate
- Drug Lupus:
 - Caused by isoniazid, hydralazine, procainamide, chlorpromazine, anticonvulsants
 - Lung and skin effects greater than renal and CNS
 - ENA anti-histone more likely to be positive
 - Remits if drug stopped
 - Sulfonamides and the Pill may exacerbate idiopathic SLE
- Discoid lupus = skin involvement only. See Discoid Lupus Erythematosus (DLE), page 330

Sjogren's Syndrome

- = Dry eyes, dry mouth and associated with rheumatoid arthritis
- Epidemiology: onset 15 – 65 years, more common in women
- Types:
 - Primary (ie no other connective tissue disease)
 - Secondary: associated with other connective tissue diseases: Rheumatoid (50% of Sjogren's have RA), SLE, Scleroderma, Polymyositis, Primary biliary cirrhosis (ie autoimmune disorders), graft-versus host disease, AIDS
- Presentation:
 - Gritty, sore eyes: keratoconjunctivitis sicca (↓lacrimation → dry eyes)

- Dry mouth: xerostomia (\downarrow salivation) – can't swallow, need sips of water at night, enlarged tender parotids
- Also dry nose, vagina
- Tiredness/depression
- Arthritis as in SLE
- Raynaud's
- Pulmonary fibrosis, pleurisy
- Also peripheral neuropathy, renal involvement, hepatosplenomegaly, pancreatitis, etc
- Compared to RA:
 - ANA is more strongly positive in Sjogren's
 - Arthritis is not destructive
- Investigations:
 - Schirmer test: < 10 mm of filter paper under the lower eye lid is wet after 5 minutes
 - ↑ESR & CRP. May have normal CRP (can get this in most CTDs, but not RA)
 - 100% have RF
 - ANA positive in 60 – 70%
 - Anti-Ro (SSA) and Anti-La (SSB) present in 70% of primary, and 10% of secondary. NB Ro and La antibodies cross the placenta causing congenital heart block
- Pathology:
 - Connective tissue disease
 - Lymphocytes and plasma cells infiltrate secretory glands (also skin, lungs and liver) causing fibrosis
 - Inflammation and destruction of exocrine glands: especially saliva and tears, with CD4+ lymphocytes
 - HLA DR3 association
- Treatment
 - Artificial tears and saliva
 - Hydroxychloroquine and methotrexate

Progressive Systemic Sclerosis (PSS)

- Connective tissue disease with inflammation, vasculitis and fibrotic changes in skin and viscera
- Epidemiology: female = 3 * male. Any age, but peak is 30 – 50 years
- Pathology:
 - Small vessel damage + oedema → collagen laid down → fibrosis and contraction
 - Dilation of other vessels → telangiectasia
- Presentation:
 - Raynaud's (90%) may precede other signs by years
 - Then swelling of fingers and hands
 - Then skin gets tight, waxy and tethered (eg fingers – pointy fingers, forearms, face – no wrinkles, pointy nose)
 - Other: telangiectasia, nail bed spots, symmetrical polyarthritis
- Types:
 - Diffuse/Generalised Progressive Systemic Sclerosis: widespread skin involvement with early visceral involvement → kidney (proteinuria, sediment, maybe crisis ↑↑BP), polyarthritis, myopathy, lung fibrosis (\downarrow expansion + \downarrow gas transfer → SOB) and GI fibrosis
 - CREST Syndrome (probably very different disease entity to Diffuse): Calcinosis (subcutaneous calcium deposits on hands) + Raynaud's phenomenon + disordered oesophageal motility (heart burn and dysphagia) + sclerodactyly (Scleroderma of the hands) + telangiectasia. Centromeric ANA
 - Limited Scleroderma:
 - Tightening and fibrosis of the skin: proximal skin scleroderma (eg face – can they open their mouth wide, any wrinkles – if so then no involvement. Limited mouth opening = microstomia) or any 2 of sclerodactyly (can they make a fist, Prayer sign: can they oppose palmar MCP joints), digital pitting scars, pulp loss, bibasilar lung fibrosis. Late visceral involvement
 - Scleroderma limited to the hands and maybe face ('Limited Scleroderma') is probably a presenting symptom of CREST syndrome even if the other features aren't present
 - Morphoea (localised skin sclerosis) rarely, if ever, progresses to PSS

- Investigations:
 - FBC: normocytic anaemia, haemolytic anaemia
 - ↑ESR
 - ANA positive in 75%. May have autonuclear autoantibodies in any of these three forms to: topoisomerase (Scl-70), RNA polymerases and centromeres. Anticentromere (ACA) in Limited and CREST. AntiScl-70 in diffuse.
 - RF +ive in 30%
 - 24 hour urine
 - Hand x-ray. Can get distal phalanges resorption
 - Barium swallow and CT of lung
- Treatment:
 - No cure
 - Education, support groups, etc
 - Raynaud's: warmth and vasodilators (Ca blocker)
 - Oesophageal mobility: omeprazole, cisapride, reflux prevention
 - Renal & Raynaud's: ACE inhibitors
 - Scleroderma: D-penicillamine (antifibrotic) or immunosuppressants (little efficacy from steroids)
- Prognosis: Limited disease has 70% 10-year survival; diffuse has 55% 10-year survival. Death from lung/renal effects

Mixed Connective Tissue Disease

- Features of SLE, PSS and polymyositis
- Anti-RNP (ribonuclear protein) +ive without other types of ANA

Polymyositis and Dermatomyositis

- Peaks in age 10-14 (mainly dermatomyositis) and 45 – 60 years (mainly polymyositis). Rare
- Presentation:
 - Voluntary muscle inflammation → *insidious*, symmetrical, proximal muscle weakness (shoulders, hips, trunk, neck – compared to polymyalgia rheumatica which just has stiffness). May → atrophy and contractures
 - Skin (only Dermatomyositis): Gottron's lesions: erythematous plaques or macules over MCP joints, extensor knees, wrist and elbows. Rash over upper chest, neck, etc
 - Other symptoms: Fatigue, malaise, weight loss, fever
 - Causes dysphagia, dysphonia, facial oedema, respiratory weakness
 - Also Raynaud's, lung involvement (interstitial fibrosis), polyarthritis, retinitis, myocardial involvement, purple rash on cheeks and light exposed areas
- Differential Diagnosis:
 - Infection
 - Muscular dystrophy
 - Endocrine: thyroid, PTH, ↑Ca, ↓K
 - Neurology: motor neurone, Guillain Barre, Myasthenia Gravis
 - Drugs
- Investigations:
 - ↑ESR, CRP, CK, maybe ↑AST and LD
 - RF positive in 50%
 - ANA may be +ive, as well as myositis specific antibodies (eg AntiJo-1 – linked to HLA DR3)
 - EMG → denervation and myopathy (not usually done)
 - Biopsy: inflammatory muscle infiltrate + fibrosis
- Associations:
 - Other autoimmune rheumatological diseases
 - Malignancy in 10%
 - Coxsackie virus, rubella & influenzae
- Diagnosis of exclusion
- Treatment: rest, steroids, methotrexate, Ig, active graded exercise between attacks

Polymyalgia Rheumatica

- Old ladies with morning stiffness in proximal muscles +/- mild polyarthritis, depression, fever, anorexia, maybe jaw claudication, angina, hypopituitarism, *not* weakness

- May be features related to underlying CTDs (arthritis if superimposed RA, headache in GCA ⇒ ask about headaches, visual disturbance etc)
- ?Syndrome with many underlying causes (eg variety of connective tissue diseases)
- Differential:
 - RA with onset of central joints
 - Frozen shoulder
 - Carcinomas: breast, thyroid, prostate
 - Myeloma
 - Polymyositis
 - Bacterial endocarditis
- Investigations: ↑ESR, anaemia, no abnormality on X-ray, usually RF and ANA negative, CK *not* usually raised, liver involvement → ↑ ALP
- Treatment: dramatic response to low dose steroids (eg 15 mg/day)

Vasculitis

- Associations:
 - Occurs in non-organ specific autoimmune diseases (eg RA, SLE)
 - Principal feature of other connective tissue diseases that may or may not be autoimmune
 - Also occurs in conditions not usually included in connective tissue diseases (eg drug reactions)
- Types:
 - Large vessel vasculitis: Giant cell arteritis, Takayasu's arteritis
 - Medium sized vessels: Polyarteritis Nodosa (PAN), Kawasaki's disease
 - Small vessel vasculitis: Wegener's Granulomatosis, Microscopic Polyarteritis, Henoch-Schonlein purpura

Giant Cell Arteritis/Temporal Arteritis

- Medium and small arteries (especially temporal arteries → medical emergency – affects retinal arteries).
- From 50 years, peaking at 75.
- Clinical: Initially persistent headache, then superficial pain and tenderness over temporal arteries, unilateral visual disturbance, arthritic pain, jaw claudication, fever, malaise, ↑ESR (Age and ESR both over 60 in 3/4 cases)
- Immune reaction with internal elastic lamina
- Diagnosed by biopsy showing giant cells engulfing the IEL and inflamed media. Biopsy is critical as treatment should continue for 2 years and therefore want to be sure of diagnosis
- Presumptive treatment with steroids. Immediate risk is blindness, but longer-term morbidity is due to steroid treatment!
- Overlaps with Polymyalgia Rheumatica in 25% of cases (→ stiff proximal muscles in the morning). See Polymyalgia Rheumatica, page 281

Polyarteritis nodosa

- Affects young adults. M:F = 4:1.
- Presents with non-specific symptoms – fever malaise, abdominal pain, renal failure, purpura.
- Immune complex mediated arteritis (type 3 hypersensitivity)
- 40% associated with Hep B
- Necrotising vasculitis of medium sized arteries (not arterioles). Involves smaller arteries – kidney, heart, liver, GI. Often patchy distribution. Macroscopic: small nodules. Microscopic: fibrinoid necrosis, intimal proliferation, media destruction, inflammation of adventitia, scarring if chronic.
- Investigations: FBC, biopsy of affected organ, ECG, ANCA may be +ive
- Treatment: steroids/immunosuppressives (azathioprine/cyclophosphamide)

Kawasaki Disease

- = Mucocutaneous Lymph Node Syndrome ~ Childhood Polyarteritis Nodosa
- Immune mediated injury to vascular endothelium, including coronary artery arteritis
- ?post viral
- Fever in kids (usually < 5) for > 5 days with bilateral, non-purulent conjunctival infection, oral mucosal changes, cervical lymphadenopathy, changes in the extremities (eg swelling of hands), & generalised rash
- Investigations: Echo for coronary aneurysm, FBC (↑WBC, ↑platelets), ↑CRP

- Differential: Scarlet fever, EBV
- Complications: pancarditis, aneurysms or dilatation
- Treatment: none, or high dose IgG/steroids

Wegener's Granulomatosis

- Generalised necrotising arteritis of small-medium sized arteries of the respiratory tract and kidney with non-caseating granuloma formation
- Wegner's triad: aseptic necrosis of the lower and upper respiratory tract and focal glomerulonephritis of the kidney
- Presentation:
 - Upper airways disease (chronic rhinitis/epistaxis/sinusitis/mouth ulcers) unresponsive to therapy. CXR shows spots. May have haemoptysis. Progresses to ulceration of nasal mucosa, perforation of the septum, heavy nose bleeds, granulomatous invasion of large bronchi → bronchial stenosis
 - Glomerulonephritis. If untreated then slow progression to end stage renal failure
 - Systemic: fever, night sweats, weight loss, et
 - Non-deforming arthritis and arthralgia
- Progression highly variable
- Investigations:
 - ↑ESR, c-ANCA positive, CXR (nodular masses, cavitation)
 - Renal biopsy: necrotising glomerulonephritis: may be focal and crescentic. Immunofluorescence is -ive ⇒ pauci-immune
- Treatment: steroids +/- cyclophosphamide → 90% remission but frequent relapse. Continue for a year then taper off

Microscopic Polyarteritis

- Vasculitis of small-medium sized vessels
- Multisystem involvement including glomerulonephritis
- Kidney involvement: crescentic rapidly progressive GN common, no immune deposits on immunofluorescence (ie pauci immune)
- Biopsy: fibrinoid necrosis and cellular proliferation within capillaries
- Frequently positive for p-ANCA
- Treatment: similar to Wegener's

Henoch-Schonlein Purpura

- Leukocytoclastic vasculitis of small vessels with deposition of IgA immune complexes in the skin, gut and kidney
- Usually in young children, associated with URTIs
- Palpable purpuric rash over the buttocks and ankles, abdominal pain and arthralgia
- Renal involvement: macroscopic or microscopic vasculitis, mesangial proliferative glomerulonephritis, maybe crescentic, IF +ive for mesangial IgA deposition
- Usually self-limiting, otherwise steroids

Others

- **Hypersensitivity angiitis** (Leukocytoclastic vasculitis): Type 3 immune injury. Associated with medicines, lupus, HBV. Microscopically: neutrophils, fibrinoid necrosis
- **Takayasu's arteritis**: Aortic thickening with autoimmune granulomas = Pulseless Disease. Rare, in young females, hypertension, pain of affected artery
- **Thromboangiitis Obliterans** = Buerger's disease. Neurovascular bundles – mainly in legs and arms of young/middle aged smokers – become inflamed and thrombosed
- **Behcet's Disease**: Systemic vasculitis, commoner in Turkey and Japan, oral and genital ulcers, eye lesions, arthritis of knee, ankles, wrists and elbows

Pain Syndromes

Chronic/Complex Regional Pain Syndrome (Type I)

- = Reflex Sympathetic Dystrophy
- =Algodystrophy
- Can develop as a consequence of trauma affecting the limbs with or without obvious nerve lesion

- Cause: ?peripheral sympathetic over-activity, pathological interaction of sympathetic and afferent systems
- Presentation:
 - Pain
 - Abnormal blood flow (cold or hot) and sweating (including distal to the trauma)
 - Structural changes eg muscle wasting (over months to years can → contractures)
- Treatment: difficult: pain relief, rehabilitation, physio, early refer to pain management clinic

Fibromyalgia

- Aetiology: unknown
- Presentation:
 - Diffuse musculoskeletal pain (over all 4 quadrants and axial) but normal muscle power
 - Morning stiffness
 - Paraesthesia
 - Tender points over the body
 - Skin fold tenderness
 - Sleep disturbance, fatigue and vertigo
- ESR usually normal
- Associations: Raynaud's phenomenon, anxiety/depression, IBS
- Diagnosis: based on finding a number of separate, defined tender points
- Treatment: analgesics and exercise

Plastic and Reconstructive Surgery

- Restoration of function and correction of deformity
- Resulting from trauma, neoplasia, etc
- Largely about transferring tissue
- Techniques:
 - Direct closure
 - Graft: gets blood supply from wound site
 - Flaps: brings blood supply with it (especially over bony prominences, and if further surgery will go through it again)
 - Tissue expansion
- Always:
 - Repair in layers
 - External layers everted (if inverted then retraction → depression)
- Burns: See Burns, page 486
- See Mr Tan's very interesting but non-examinable hand-outs

Accident Compensation Corporation (ACC)

- Provides economic support for injured people and aims to reduce the physical impact of injury
- Is a no fault, compulsory scheme
- NZers gave up right to sue in return for specified support
- Resources available:
 - Costs of retrieval from accident scene
 - Costs of diagnosis and physical rehabilitation
 - Compensation for loss of earnings (80% of pre-injury income after 1 week off work)
 - Vocational support: retraining if necessary to return to work
 - Range of personal support to help make living with an injury more comfortable

Haematology and Immunology

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Haematology Overview

Cell/System	Disorders
Anaemia	Microcytic: Iron Deficiency, Thalassemia, Chronic Disease (can be normocytic) Macrocytic: Alcoholism, ↓B12/folate (Megaloblastic), Newborn. Also liver disease, marrow disorders, drugs, malaria, idiopathic
Pancytopenia	Aplastic Anaemia Also alcohol, bone marrow infiltration, megaloblastic anaemia, hypersplenism
Other Red cell	Spherocytosis, Hb abnormalities
Hypocoagulation	Haemophilia A & B, Von Willebrandt's, DIC Also liver disease, ↓Vit K, Renal failure, iatrogenic (aspirin, heparin)
Hypercoagulation	Primary: Factor V Leiden, ↓Antithrombin 3, ↓Protein C & S Secondary: Malignancy, pregnancy, stasis, age, myeloproliferative diseases
Thrombocytosis	Reactive: Infection, inflammation, bleeding, malignancy, splenectomy Primary: Essential thrombocythaemia
Thrombocytopenia	Immune thrombocytopenia, Heparin induced, artefact, dilutional, marrow production failure, peripheral consumption (drugs, DIC, etc) Mainly acquired: aspirin, uraemia, paraproteinaemias
Platelet function disorders	
Myeloproliferative	Chronic Myelocytic Leukaemia, Acute Myelocytic Leukaemia, Polycythaemia Rubra Vera, Essential thrombocythaemia, Myelofibrosis
Myelodysplasia	
Lymphoproliferative	Chronic lymphocytic leukaemia, acute lymphocytic leukaemia, multiple myeloma

- Also see Blood Tests, page 9
- Also see Blood Products, page 552 (including transfusion)

Microscopy of Abnormal Cells

Red Blood Cells

- Oval macrocytes + hypersegmented neutrophils ⇒ megaloblastic anaemia (B12/folate)
- Target cell RBCs (haemoglobin in the middle – non-specific): most commonly seen in patients with liver disease (eg too much alcohol)
- Small pale RBCs, target cells + pencil poikilocytes (elongated RBCs) ⇒ iron deficiency
- Rouleaux: red cells stack like coins, fall fast if high ESR. Stick together due to ↑immunoglobulin or fibrinogen). Causes: inflammation, myeloma
- No lighter patch in middle ⇒ spherocytes
- Spherocytosis: if only some RBCs, then spleen has taken out a bit of membrane ⇒ autoimmune haemolytic anaemia. If all RBCs are spherocytes then hereditary spherocytosis. If spherocytes + reticulocytes then spherocytic anaemia
- Cygnet shape (ring form with blue circumference) inside cell ⇒ malaria parasite
- Tear drop red cells ⇒ myelofibrosis or polycythaemia
- ↑ Polychromasia ⇒ some red cells a bit blue due to stain – still contain some RNA
- Reticulocytes: normal is 0.2 – 2%. Look big and blue. Will be high in anaemia (except ?anaemia of chronic disease)
- Howell-Jolly Bodies: Little purple/black dots (like a ball bearing) in RBC = remnant DNA that hasn't been removed by the spleen. Seen in splenectomy patients
- Fragmented cell: red cell sliced in circulation (DIC, artificial heart valve)

White Blood Cells

- Normal lymphocyte: small, little/no cytoplasm
- Neutrophils have multilobed nuclei, ≥ 6 lobes is hypersegmented (megaloblastic anaemia: B12, folate. Also drugs, chemotherapy, renal failure)
- Plasma cell: eccentric nuclei, clock-face chromatin. If eccentric nucleus (clear area next to nucleus) in bone marrow ⇒ multiple myeloma

- Neutrophil maturation:

Blast	No granules, fine chromatin	Large
Myelocytes	Large round nucleus	Large
Metamyelocytes	Large bean shaped nucleus	Large
Band	Horse shoe shaped nucleus	Smaller
Neutrophil	Segmented neutrophil, dense chromatin	Smaller

- Normal differentiation: Neutrophils 80%, Lymphocytes 20%
- Lymphocyte: Toxic Changes (i.e. 'switched on'): ↑ granules, vacuoles, Dohle bodies (blue clumps in cytoplasm), nuclear clumping. Strong indicator of bacterial infection
- If high lymphocytes and lots of 'atypical lymphocytes' then viral infection: EBV, HIV, CMV
- Auer rods in a blast ⇒ acute myeloblastic leukaemia
- Eosinophil: normal is reddish cytoplasmic granules. ↑ In toxoplasmosis, allergy (asthma, drugs, etc), gut parasites
- Bone marrow biopsy: normal is about ½ fat, ½ cellular

Leukaemias

- Smudge cells ⇒ CLL. Middle aged, significant lymphadenopathy
- ↑WCC, enlarged lymph nodes, splenomegaly, lots of white cells, majority are mature neutrophils ⇒ CGL (= CML)
- Acute leukaemias: cells not mature

Anaemias

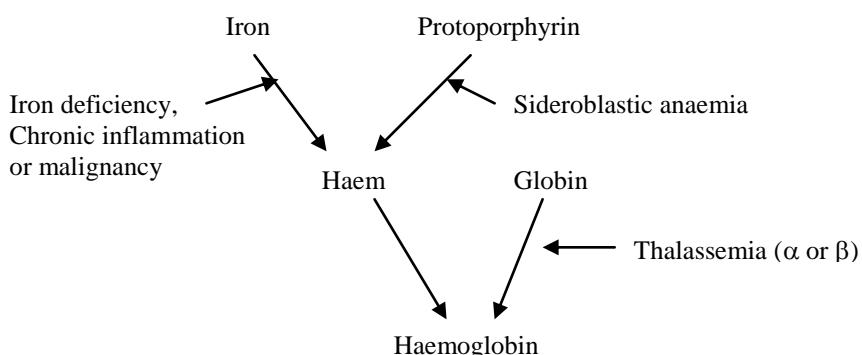
- = Hb level below normal for age and sex
- Normal Hb levels:
 - Male 138 – 180 g/l
 - Female 115 – 165 g/l
- Mild is > 100
- Moderate is 80 – 100
- Severe is < 80
- Symptoms
 - SOB on exertion
 - Tiredness/fatigue
 - Lack of concentration
 - ↓O₂ delivery → Bring on underlying angina or pain/claudication in legs
- Signs: Pale conjunctiva, palmar creases, nail beds: but insensitive test

Microcytic Anaemia

- = MCV < 75 fl (normal is 76 – 98)

Causes

- Iron deficiency anaemia
- Thalassemia
- Chronic disease (see Anaemia of Chronic Disease, page 291)
- Other Causes: Sideroblastic anaemia, lead poisoning



Iron Deficiency Anaemia

- See also Iron Deficiency, page 646 for Iron Deficiency Anaemia in Children
- Commonest cause of anaemia
- 15-25% of healthy pre-menopausal women have low ferritin
- 2 mls of blood = 1 mg of iron. Easy to get anaemia from a small trickle bleed
- Average menstrual loss = 60 ml
- Iron absorption:
 - Western diet contains 10 – 15 mg iron
 - 5 – 10 % normally absorbed
 - 20 – 30% absorbed in Fe deficiency and pregnancy
 - Absorbed in duodenum, proximal jejunum
- Iron transport and storage:
 - Fe carried by Transferrin (MW 80,000): made in liver, T½ 8 – 10 days
 - Ferritin: Water-soluble protein – MW 465,000. Stores iron in cells. Is proportional to body iron stores
- Clinical features of iron deficiency:
 - Anaemia
 - Glossitis: swollen tongue, sore, lost papilla
 - Koilonychia: spoon shaped nails
 - Dietary cravings (pica): eating strange stuff – kids eat dirt, pregnant women eat ice
 - Blue sclera: highly specific
 - Pharyngeal webs → dysphagia
- Diagnosis:
 - Microcytic hypochromic anaemia: use MCV (not MCH – but highly correlated)
 - On film may see: target cells (haemoglobin in middle – non-specific), pencil poikilocytes, ↑ platelets
 - Lab findings: ↓ serum ferritin (sufficient on its own) – will also see ↓ serum Fe (but Serum Iron useless) and ↑ transferrin/ICP (Iron combining protein). Mean cell volume in normal range may disguise a combination of small Fe deficient cells plus lots of large reticulocytes

Macrocytic Anaemia

- = MCV > 96 fl

Causes

- New born
- ↓B12/folate
- Alcoholism (most common cause but usually mild)
- Liver disease
- Primary marrow disorders
- Drugs
- Malaria
- Idiopathic/others

Megaloblastic Anaemia

- Is NOT the same as macrocytic anaemia
- Causes:
 - ↓Folate (comes from veges)
 - ↓B12 (comes from meat)
 - Drugs that interfere with B12 metabolism
- Leads to defective DNA synthesis and delayed maturation of the nucleus cf. cytoplasm.
- Big red cells and hyper-segmented neutrophils (>= 6 segments)
- Clinical features:
 - Anaemia
 - Infection (↓neutrophil function)
 - Jaundice (↑bilirubin)
 - Purpura
 - Malabsorption (↓gut lining)
- Lab features:

- MCV > 95 fl
- Oval macrocytes
- ↓WBC and ↓platelets
- Investigations: blood film and B12/folate levels. Serum folate is useless – folate is stored in RBCs
- If low B12:
 - Also have symmetrical peripheral neuropathy
 - Could be diet: if ↓↓animal products
 - Could be malabsorption: pernicious anaemia. Check intrinsic factor antibodies against gastric parietal cells. Schilling test for absorption
- If low folate:
 - Not eating enough veges (e.g. living on tea and toast)
 - Exclude malabsorption (e.g. Celiac Disease)
 - Review drugs

Pancytopenia

Stem Cells

- Blood stem cells detected by CD34+
- Live in bone marrow: biochemical environment there necessary for survival – from fat, fibroblasts, endothelial & macrophage cells

Pancytopenia

- Confirmed ↓RBC, ↓WBC and ↓platelets
- Causes:
 - ↓Production:
 - Bone marrow infiltration/failure
 - Megaloblastic anaemia
 - Miscellaneous (e.g. alcohol)
 - Aplastic/hypoplastic anaemia
 - ↑Margination: Hypersplenism

Aplastic Anaemia

- Rare
- Defect in supportive environment: dysfunctional stem cells, autoimmune damage
- Criteria for severe:
 - Neutrophils < 0.5
 - Platelets < 20
 - Reticulocytes < 10 * 10E9
 - Hypocellular marrow
- Causes:
 - Idiopathic
 - Drugs/chemicals
 - Radiation
 - Viral
 - Pregnancy
- Treatment:
 - Supportive care
 - Immunosuppressive treatment
 - Stem cell transplantation

Hereditary Spherocytosis

- Normal RBC has surplus membrane → floppy
- Spherocytes have less membrane → tight
- Autosomal dominant
- Could take out spleen if symptomatic

Hb abnormalities

- = Synthesis of abnormal Hb or ↓rate of synthesis of normal α or β globin chains

Syndrome	Abnormality
Haemolysis	Crystalline Hbs (S, C, D, E) → unstable Hb
Thalassemia	α or β, due to ↓globin chain synthesis: Thalassemia major – transfusion dependent, homozygous β0, Mediterranean, splenomegaly, frontal bossing of forehead, bad teeth Thalassaemia intermedia
Familial Polycythaemia	Thalassaemia minor - β0 trait - ↓MCV. α0 trait - ↓MCV, Hb H bodies, target cells
Methaemoglobinaemia	AH1, measure P 50 for O ₂
	Failure of reduction

Data Interpretation

- Pregnancy → ↑Fe requirements and ↑fibrinogen (→ ↑ESR)
- If mild microcytic anaemia and normal ferritin it's not iron: check either Thalassaemia or anaemia of chronic disease
- Ferritin is an acute phase protein. It will be raised in chronic disease. So if there is chronic inflammation and a low-normal ferritin, the underlying ferritin is likely to be below normal
- Mildly ↑MCV could be because of ↑reticulocytes → check haemolysis
- Haemolysis tests:
 - ↑Production: reticulocytes, blood film
 - ↑Breakdown: Hb and Hatoglobins (binding protein for haem – used up in haemolysis → would fall)
 - Combes test: is there antibody on the RBC
 - If Fe in urine (Urine haemosiderin) then intravascular haemolysis (not spleen – which is extravascular). E.g. aortic valve replacement → haemodynamic/shear stress from turbulent flow

Porphyria

- Disorder of haem synthesis → toxic metabolites
- Many types, all due to genetic deficiency. Homozygous not viable. Heterozygotes can produce enough haem, but when the system is challenged → ↑ toxic metabolites
- Symptoms:
 - Uncommon, but differential in intermittent abdominal pain
 - Can be intermittent or constant
 - Can acutely cause psychotic symptoms
 - Sun sensitivity (accumulation of metabolites in skin)
 - Neuro-visceral symptoms (pain but no organ pathology)
 - Rare types can cause sideroblastic anaemia
- Investigations:
 - Urine test for metabolites (porphyrins)
 - Then specific test for which porphyria
- ALA synthase controls the rate limiting step at the beginning of the pathway:
 - Induced by: BZDs, alcohol, oestrogen and progesterone (→ onset at puberty or on starting the OCP), sulphonamides, tetracycline, theophylline
 - Inhibited by haem, glucose

Haematology of Systemic Disease

- Also see Hypercoagulable States, page 293
- E.g. Cancer → ↑ESR, ↑Neutrophils, ↑coagulation, anaemia

Erythrocyte Sedimentation Rate (ESR)

- Normal varies by age and sex (increases with age)
- Rouleaux: red cells stack like coins, fall fast
- Due to:
 - Acute phase reactants: esp. fibrinogen
 - Gamma globulins
 - Anaemia

- Clinical uses: collaborative test, monitor course of disease
- ↑ESR in pregnancy, infection, tumours, connective tissue disorders, multiple myeloma

Leucocytosis

- Normal range varies with age (esp. kids)
- Neutrophils:
 - In adults: $2 - 7.5 \times 10^9$
 - Lobed nucleus, lots of granules in cytoplasm
 - Made in marrow, transported via blood
 - Neutrophilia in many states, not just infection, and including stress. Physiological neutrophilia e.g. exercise → ↓margination

Lymphocytosis

- In acute infections: pertussis, infectious lymphocytosis, EBV, viral hepatitis
- In chronic infections: brucellosis, Tb, Syphilis
- In haemopoietic disorders
- Toxic Changes (i.e. ‘switched on’): ↑granules, vacuoles, Dohle bodies (blue clumps in cytoplasm), nuclear clumping. Strong indicator of bacterial infection

Anaemia of Chronic Disease

- Causes:
 - Chronic infections e.g. TB, SBE, AIDS
 - Chronic inflammatory states e.g. RA, ulcerative colitis
 - Recognise it so patient is not over-investigated
- Features:
 - Mild to moderate anaemia: $70 - 100 \text{ g/L}$ (usually $90 - 100$)
 - Normocytic to mild microcytosis
- Differential diagnosis
 - Fe deficiency
 - Renal impairment
 - Marrow infiltration
 - Haemolysis
- Iron Studies (highly examinable):

	Fe deficiency	Chronic Disease
Serum Iron	↓	↓
Iron Binding Capacity	↑	↓
%Saturation	↓	↓
Marrow Iron	↓	↑
Serum Ferritin	↓	N or ↑

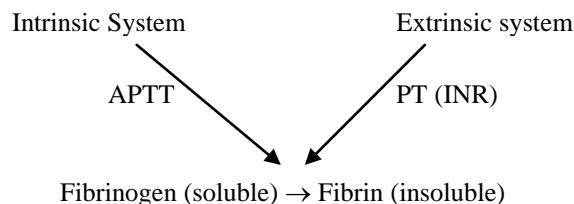
- Blood results in chronic disease:
 - ↑Ferritin
 - ↓Protein (especially albumin)
 - ↑Globulins
- Pathogenesis
 - ↑RBC destruction → ↓survival
 - ↓Iron metabolism
 - Impaired erythropoietin response
 - Cytokines (TNF-α, IL-1, interferons)
- Treatment
 - Won’t respond to iron, etc
 - Treat underlying cause
 - Erythropoietin (but very expensive)

Haemostasis

- Necessary factors for haemostasis (stopping bleeding):
 - Vasoconstriction
 - Platelets
 - Coagulation (= fibrin production)

Coagulation

- Key reaction: fibrinogen → fibrin



- Intrinsic pathway:
 - XII → II via IX and VIII
 - Triggered by damage to endothelium
 - Measured by Partial thromboplastin Time (PTT) = Activated PTT (APTT). Also called PTTK
 - Reduced by heparin treatment
- Extrinsic Pathway:
 - VII → II
 - Triggered by chemicals extrinsic to blood stream
 - Measured by Prothrombin time or INR (International Normalised Ratio): ratio of Patient PT to Control. Normal < 1.3. INR mainly measures top end of the extrinsic pathway – so INR may not be affected by heparin even though it affects the common pathway. APPT more sensitive to ↓common pathway
 - Reduced by warfarin treatment

Hypo-Coagulation Diseases

- Congenital:
 - Haemophilia A
 - Haemophilia B
 - Von Willebrand's Disease
 - Rare factor deficiencies
- Acquired:
 - Liver diseases → ↓coagulation factors
 - DIC
 - Vitamin K deficiency: needed for factors 2, 7, 9 and 10
 - Uraemia: renal failure → ↓platelets and coagulation function
 - Massive blood transfusions → dilution of clotting factors
 - Factor inhibitors

Von Willebrand's Disease

- ↑Bleeding time, ↑APTT due to ↓ VIII (VW factor is a binding protein for VIII)
- Symptoms: Superficial bleeds – mouth, nose, gut, bruising, heavy menstrual bleeding
- Autosomal dominant
- Comes in mild, moderate and severe forms

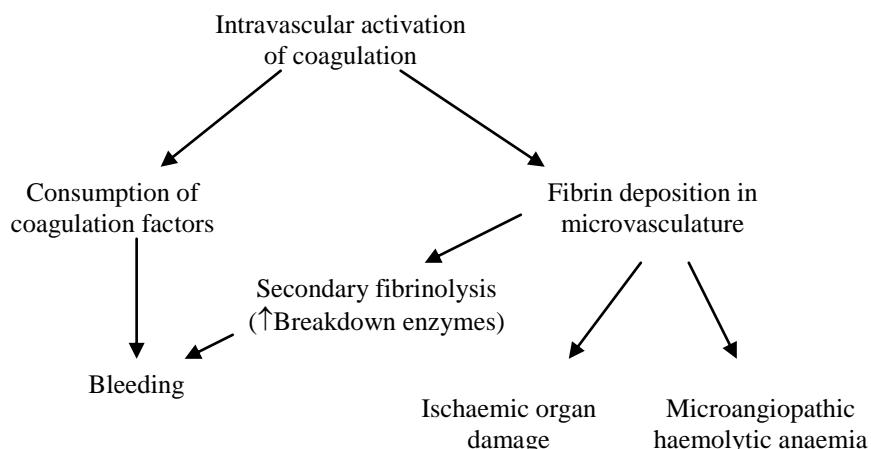
Haemophilia

- Ratio of 4:1 of A (↓factor VIII) to B (↓factor IX)
- Prevalence of 13 – 18 per 100,000 males in Wellington (high)
- Symptoms: bleeding into soft tissues, joints, dental extraction. Deep bleeds → major orthopaedic implications. NOT superficial or gut
- Classification:
 - Severe: < 1% - joint bleeds, e.g. once a fortnight or month
 - Moderate: 1 – 4 % - some joint bleeds, main problem with trauma, not spontaneous bleeds
 - Mild: 5 – 25% - main problem trauma
- Lab diagnosis:
 - INR: normal
 - APTT: prolonged
 - Fibrinogen: normal
 - Platelets: normal

- Bleeding time: normal
- Factor assay reduced (do VIII first then IX)
- Symptoms of a joint bleed:
 - Strange sensation: not really a pain – treat at this point, they will know despite no signs yet
 - Swelling
- Treatment:
 - Factor replacement: either prophylactic or on demand
 - Choice of factor product: blood derived or recombinant
 - Management of inhibitors

Disseminated Intravascular Coagulation (DIC)

- = Laying down fibrin inappropriately within vasculature
- Causes:
 1. Activation of extrinsic system by thromboplastin (triggers VII). Thromboplastin is a lipoprotein substance from cell membranes. Due to: massive injury ($\uparrow\uparrow$ release of thromboplastin), septicaemia (damage to endothelium), tumour cells breaking down
 2. Activation of intrinsic system: anoxia, acidosis, sepsis, burns
 3. Direct activation of II & X: amniotic fluid embolism, pancreatitis (\rightarrow release of toxic enzymes into blood)
- Outcomes:



- Lab screen:
 - \uparrow PT (Prothrombin time)
 - \uparrow APTT
 - \downarrow Fibrinogen
 - \downarrow Platelets
 - \uparrow Fibrin degradation products
- Treatment:
 - Correct cause
 - Platelet transfusion
 - Fresh Frozen plasma
 - Cryoprecipitate

Hypercoagulable States

- Primary Causes:
 - Factor V Leiden:
 - Most common primary cause
 - Point mutation on factor V prevents breakdown \rightarrow \uparrow levels of Va \rightarrow hypercoagulable
 - Heterozygous have lifetime risk of 30 – 40% of thrombotic event, Homozygous then 50 – 60%
 - In thrombotic patients, 20 – 40% have factor V Leiden, mainly in Caucasians
 - Prothrombin gene mutation
 - Antithrombin 3 deficiency:
 - \rightarrow Reduced breakdown of thrombin
 - Heparin co-factor, α 2 globulin

- Autosomal dominant, 1:2-5000 in Caucasian
- Found in 2 – 3 % of DVTs
- Can also cause mesenteric or brachial thrombosis. These are rare so → ↑index of suspicion
- Protein C or S deficiency
- Homocysteinaemia
- Secondary Causes:
 - Malignancy
 - Pregnancy and for 6 weeks afterwards: hypercoagulable, stasis, venous compression. If concurrent primary disorder then prophylaxis with sc heparin (warfarin contra-indicated)
 - Stasis: immobilisation, surgery, local pressure
 - Age
 - Myeloproliferative disorders
 - Antiphospholipid Syndrome (acquired, aggressive)
 - Infection
 - Trauma

Data Interpretation

- Serum = plasma that's clotted: i.e. no clotting factors
- Citrated plasma: citrate chelates calcium – so can't act as a co-factor in clotting. Add Ca to reverse
- Aspirin for Coronary Heart Disease mimics VWD. (i.e. ↑bleeding time, everything else normal). T½ of platelets = 3 – 4 days. Need to stop aspirin 10 days before surgery. ½ an aspirin enough to increase bleeding time. 45 minutes to have an effect after oral dose
- Heparin → ↑APPT
- Fractionated Heparin → ↑TT (APPT may be normal)
- Warfarin → ↑INR
- Try to determine deficiency (e.g. FVIII or Warfarin → ↓2,7,9,10) or Inhibition (e.g. aspirin, heparin)

Platelets and Platelet disorders

Platelets

- No nucleus: contain granular cytoplasm
- Normal count: 150 – 400 * 10E9/L
- Normal size: 2 – 3 um
- From megakaryocyte in bone marrow (from pluripotential stem cell under the influence of thrombopoietin)
- Lifespan 10 days – destroyed mainly in spleen. 20 – 30% of total body platelets are pooled in spleen
- Function – form haemostatic plug:
 - Adherence: via Ia, indirectly via Ib & VWF
 - Shape change
 - Release reaction
 - Aggregation: glycoprotein IIb/IIIa via fibrinogen
- Bleeding time: time taken for a standardised skin incision to stop bleeding at venous pressure of 40 mmHg. Normal is 1 – 7 minutes. Depends on platelet numbers, platelet function, vascular factors (e.g. connective tissue disorders)
- Disorders:
 - Thrombocytosis: too many
 - Thrombocytopenia: too few
 - Functional disorders

Thrombocytosis

- = > 400 *10E9/l
- Causes:
 - Reactive: infection, inflammation, bleeding, malignancy, splenectomy, Fe deficiency, haemorrhage. Treat underlying disorder. Not usually necessary to treat platelets, but if so then aspirin
 - Myeloproliferative: primary or essential thrombocythaemia – largely diagnosis by exclusion
- Increased risk of venous and arterial thromboses

Thrombocytopenia

- = $<150 \times 10^9/L$
- Symptoms: bleeding in skin & mucosal surfaces, petechiae (<1 mm), purpura (1-5 mm), ecchymoses (>5mm), menorrhagia. Bad bleeding (e.g. in stools) usually only becomes significant below platelet count of 10
- Causes:
 - Artefact (e.g. clot in sample – usually due to using EDTA tube not citrate)
 - Dilutional thrombocytopenia: splenomegaly, massive blood transfusion
 - Marrow production failure (low platelet count & reduced/absent megakaryocytes):
 - Component of pancytopenia
 - Isolated thrombocytopenia: alcohol, chlorthiazides, rare megakaryocytic hypoplasias
 - Peripheral consumption (more common – low platelet count, but normal/increased megakaryocytes):
 - Immune:
 - Idiopathic thrombocytopenic purpura
 - Secondary to drugs (e.g. quinine, heparin), autoimmune disease (SLE), CLL, virus (e.g. HIV)
 - Non-immune:
 - DIC
 - Haemolytic uraemic syndrome

Immune Thrombocytopenia (ITP)

- Autoantibodies or immune complexes bind to platelets and cause premature destruction in spleen – lifespan reduced to 1 – 2 days
- ITP does not cause splenomegaly
- Acute ITP:
 - Immune complex mediated
 - Majority of childhood ITPs
 - Often follows viral infection
 - 90% resolve spontaneously within one month
 - Rarely requires treatment
- Chronic ITP:
 - Autoantibody to platelet glycoprotein
 - Majority of adult ITP
 - Usually no preceding illness
 - 10% resolve spontaneously: need to treat, although if platelets at around 30 – 50 may not need treatment – may dip during a viral illness. Need to review pre-surgery.
- Treatment (if any needed):
 - Steroids (1 mg/kg prednisone per day). 30% don't respond
 - Intravenous immunoglobulins (swamp Fc receptors in spleen so platelets not destroyed – temporary). 30% don't respond
 - Splenectomy (see Splenectomy, page 307 for risks)
 - Review if every pregnant: antiplatelet IgG may cross the placenta

Heparin-Induced Thrombocytopenia

- 1% of patients develop a drug-dependent antiplatelet antibody
- 3% of these immune complexes bind platelet Fc receptors & induce aggregation
- Presentation is thrombocytopenia followed by thrombosis
- Can be fatal
- Management: stop heparin

Platelet Function Disorders

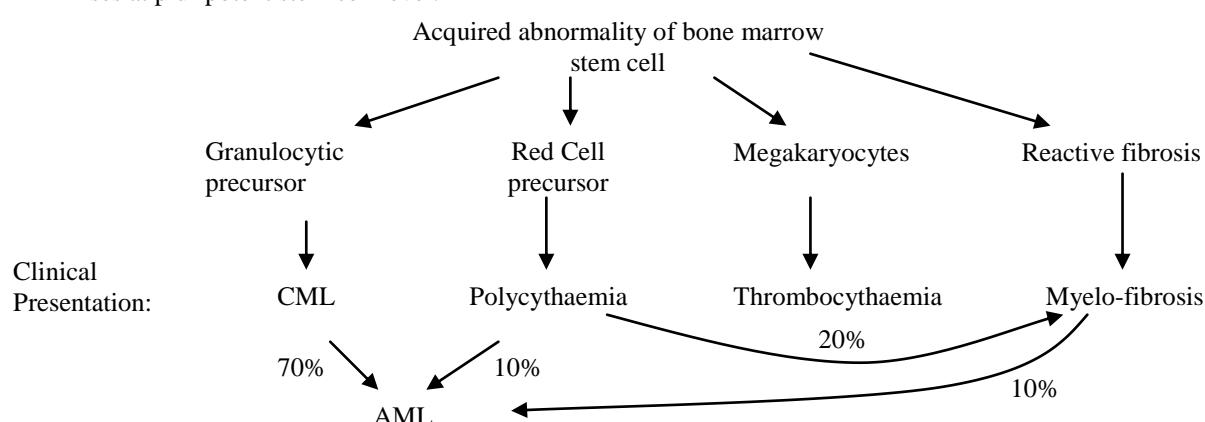
- Congenital: rare
- Acquired: common:
 - Aspirin (inhibits cyclo-oxygenase $\rightarrow \downarrow TXA_2 \rightarrow \downarrow$ aggregation)
 - Uraemia (i.e. renal failure)
 - Cardiac bypass
 - Myelodysplasia

- Paraproteinaemias

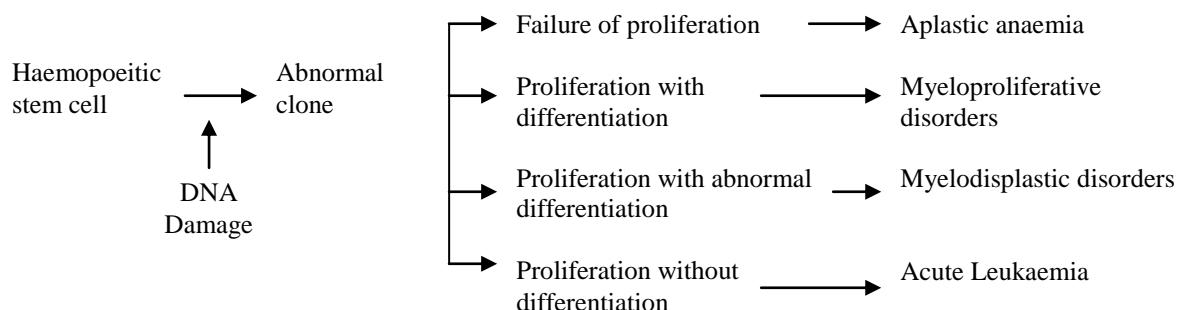
Myeloproliferative Disorders (MPD)

Introduction

- Myelo = marrow
- 4 types:
 - Polycythaemia rubra vera
 - Essential thrombocythaemia
 - Myelofibrosis
 - Chronic granulocytic leukaemia (=chronic myeloid leukaemia)
- Primary, clonal proliferation of myeloid (marrow) cells
- Arises at pluripotent stem cell level:



- Leads to mixed picture as diseases merge
- Variation is based on degree and type of proliferation:



- Leucoerythroblastosis:
 - Nucleated RBC and immature neutrophils in blood
 - Disturbance of blood/marrow barrier (normally stops immature cells getting out)
 - Causes:
 - Immature barrier: common in new born
 - Toxic: septicaemia
 - Hypoxia: respiratory failure
 - ↑↑Marrow function
 - Mechanical damage: e.g. infiltration of metastatic cancer (breast, lung, prostate go to bones)
 - Extramedullary haematopoiesis:
 - Marrow cells outside marrow (e.g. spleen, liver, lymph nodes)
 - Common in MPD, especially myelofibrosis

Polycythaemia Vera

- = Erythrocytosis

	Males	Females
Hb	> 17.5 g/dl	> 15.5
Red Cells	> 6.0 *10E11/l	> 5.5
PCV (packed cell volume)	> 58%	> 48%

- Investigation: total red cell volume by ^{51}Cr . Also erythropoietin assay
- Classification (given Raised PCV):
 - $\uparrow\text{RCM}$ (Red cell mass) = Absolute
 - Normal RCM = apparent

Primary Proliferative Polycythaemia

- Clonal stem cell disorder
- Predominant age 55 – 60 years
- Diagnosis:
 - $\text{RCM} > 36 \text{ ml/kg}$ (i.e. absolute polycythaemia)
 - No secondary cause: e.g. O₂ saturation > 92% (e.g. CORD)
- Effects:
 - Vascular complications: TIA, cerebral thrombosis, microvascular (e.g. toes), headaches, DVTs (but usually arterial problems due to \uparrow viscosity e.g. stroke)
 - Haemorrhage
 - Pruritis
 - Gout
 - Splenomegaly (also liver)
- Lab findings:
 - Hb & PCV \uparrow
 - $\uparrow\text{WBC}$ in 2/3
 - $\uparrow\text{Serum B12}$
 - Low erythropoietin
 - Platelets 400 – 800 in 50%
 - Hypercellular marrow: little fat, \uparrow in megakaryocytes
 - 'Hot' looking bone scan: lots of activity
 - Tear drop red cells
- Treatment:
 - Venesection: take off a unit of blood every 3 or 4 months (if old do it slow)
 - If \uparrow platelets as well ($\Rightarrow \uparrow$ clotting risk) then radioactive P32 (risk of leukaemia 10 years on), Busulphan & allopurinol ($\rightarrow \downarrow$ gout). Also hydroxyurea
- Course:
 - 20% progress to myelofibrosis
 - AML transition
 - ?Splenectomy if massive
 - Median survival = 8 – 15 years

Secondary Causes of Polycythaemia

- Hypoxia: normal erythropoietin. High altitude, lung disease, cyanotic CHD, smoking
- Inappropriate erythropoietin: renal tumours, renal ischaemia (auscultate for renal bruits), fibroids, hepatoma
- Miscellaneous: e.g. drugs like androgens for breast cancer

Apparent Polycythaemia

- \uparrow Packed cell volume (=PCV = Haematocrit) but normal RCM (ie RBCs a greater proportion of a unit of blood, but normal volume of RBCs in the body):
 - Diuretics
 - Alcohol
 - Hypertension
 - Early primary polycythaemia
- High altitude: initially \downarrow plasma volume then absolute polycythaemia (and O₂ curve shifts left)

Essential thrombocythaemia

- Clinical presentation:
 - Any age, usually older
 - Often asymptomatic
 - Bleeding OR thrombosis (e.g. digital arteries → necrotic toes)
 - Splenomegaly (2 – 3 cm) in 70%
- Lab results:
 - ↑Platelets, often $> 1000 * 10^9$
 - Morphology abnormal, normal plus large platelets
 - Platelet function studies abnormal
 - Hb normal or mild anaemia
 - WBC normal or mild ↑
 - Bone marrow: many megakaryocytes
- Treatment:
 - Chemotherapy: hydroxyurea
 - Radioactive phosphorous: P32 – stored in bone so zaps marrow
 - Interferon
 - Prognosis: if platelets down then good, if not then bad

Myelofibrosis

- Clinical presentation:
 - Old age
 - Preceding polycythaemia in 30%
 - Anaemia
 - Slow onset, weight loss, night sweats – insidious
 - Massive hepatosplenomegaly. Large spleen → pressure on splenic blood supply → infarction → pain
- Lab results:
 - Hb low
 - WBC high early, low late
 - Platelets high early, low late
 - Leucoerythroblastosis
 - Tear drop red cells
 - LAP (leucocyte alkaline phosphatase)
 - Philadelphia chromosome –ive
 - Fibrosis of bone marrow
- Treatment: Mainly supportive: observation, low does chemotherapy, splenectomy (symptomatic effect only)
- Prognosis:
 - Mean survival 3 – 4 years, may become transfusion dependent
 - 10% develop AML

Chronic Granulocytic Leukaemia

- = Chronic Myeloid Leukaemia
- Clinical presentation
 - Any age
 - Tired, off colour, sweats
 - Slow onset
 - Large spleen (also liver)
- Lab results:
 - ↑↑WBCs (30 – 300). In chronic there will be mature and immature blasts (myelocytes, promyelocytes and lymphocytes as well. Just a general left shift). In acute there will be immature only.
 - Bone marrow has ↑↑neutrophils
 - Philadelphia chromosome +ive
 - Low leukocyte alkaline phosphatase (LAP)
 - ↑Uric acids

- Course:
 - Chronic phase: median duration 3 – 4 years
 - Transformation (either to myeloblastic/AML or lymphoblastic) aggressive/acute – end stage
- Treatment:
 - Hydroxyurea: controls proliferation but won't stop transformation
 - Interferon: suppresses marrow, in 15% Philadelphia goes away (\rightarrow no transformation)
 - Autotransplant: use patient's stem cells
 - Allograft (use sibling): 60% cure, 20% death, 20% remission
 - MUD (Matched unrelated donor)
 - 'Mini-transplant': new stem cell technique with no high dose chemo/radiotherapy. Transplant mops up weakened immune system without you needing to kill it
 - New drug: Glevac (ST1571) – targets Philadelphia Chromosome:
 - Acquired genetic defect – 9:22 translocation \rightarrow BCR-ABL oncogene (functional oncogene) \rightarrow P210-BCR-ABL oncoprotein
 - Leads to cell proliferation, \downarrow adhesions and \downarrow apoptosis without regulation

Myelodysplastic syndromes

- Description:
 - Heterogeneous group of disorders
 - Clonal abnormality of haemopoietic stem cells
 - Abnormal, ineffective haematopoiesis
 - Involves 1 or more lineages
 - Irreversible quantitative and qualitative defects (ie normal count but bad function)
 - Tendency to evolve to acute leukaemia
- Clinical
 - Usually elderly
 - Features of bone marrow failure: tired (anaemia), bleeding, infection, mild splenomegaly in 10 – 20%
 - Incidental finding on blood film in 20%
 - 4 – 12 per 100,000 per year (definitional problems)
- Variants:
 - Refractory anaemia +/- further features (eg excess blasts)
 - Chronic myelomonocytic leukaemia
- Differential diagnosis:
 - Megaloblastic anaemia
 - Acute leukaemia
 - Heavy metal toxicity (lead, arsenic)
 - Chronic infection
 - Immune deficiency (esp HIV)
 - Anticancer chemo/radio therapy
 - Myeloproliferative disorders
 - Bone marrow hypoplasia
- Progression:
 - 70 – 80% die of marrow failure
 - 20 – 30% die of progression to leukaemia
 - Median survival varies with subtype from 6 – 50 months
- Treatment:
 - Response rates to treatment poor
 - Supportive care
 - Maybe cytotoxic chemotherapy or stem cell transplants in the few young cases
 - Growth factors eg erythropoietin
- Secondary myelodysplasia:
 - ↑Incidence
 - Complication of former treatment: alkylating agents (including cyclophosphamide, widely used as an immunosuppressive, eg in Rheumatoid arthritis) and topoisomerase II agents
 - Risk related to cumulative dose and duration of exposure
 - Peak 5 years post treatment

- Poor prognosis

Leukaemia

- Leuk: Greek for white
- = Cancer dominantly of white cells arising in MARROW. Lymphoma primarily arises in lymph nodes
- Summary:

	Acute	Chronic
Myeloblastic/Granulocytic	Neutrophil precursors Sudan black for peroxidase Auer rod in cell	Mature neutrophils and blasts Philadelphia +ive Converts to AML after 3 years
Lymphoblastic	T/B Cell precursors PAS stain for glycogen	Proliferation of mature B cells Doesn't convert to ALL Longer mean survival

Chronic Leukaemia

- Chronic Myeloblastic Leukaemia (CML): Converts to AML/AGL. See Chronic Granulocytic Leukaemia, page 298
- Chronic Lymphoblastic Leukaemia (CLL): see Chronic Lymphocytic Leukaemia, page 304. Doesn't convert to ALL

Acute Leukaemia

- Rapid onset, 100% mortality within 3 months if untreated
- Very undifferentiated (anaplastic) cells: blasts, no normal cells in blood
- Types:
 - Acute Myeloblastic Leukaemia (AML). Chance of cure with chemo alone = 20 – 40%. With transplant = 60%. Has Auer rob in blast
 - Acute Lymphoblastic Leukaemia (ALL)
- Presentation:
 - Tired due to anaemia, breathless
 - Bleeding due to ↓ platelets, nose bleeds
 - Bacterial infection
 - Hepatosplenomegaly, ↑ lymph nodes, bone pain (push on sternum)
- Investigations:
 - FBC: ↓ Hb, ↓ platelets, white count: High, normal **or** low (sometimes leukaemia cells stay in marrow)
 - Bone marrow: > 30% of nucleated cells in the marrow are leukaemic blasts
- Classification:
 - Cytochemistry:
 - Staining. PAS - +ive stain for glycogen ⇒ lymphoblastic
 - Sudan black +ive for peroxidase ⇒ myeloblastic
 - Immunology: flow cytometry
 - Cytogenetics

Treatment

- Supportive Care:
 - Antibiotics, platelet/RBC transfusion
 - Venous catheter: Hickman catheter
- Cytotoxic Treatment:
 - Complex multi-drug protocols
 - Remission induction: 1-4 weeks depending on protocol. FBC normal and < 5% blasts in marrow (that's normal). AML – achieved in 70 – 80%. ALL – achieved in 70 – 80% of adults, 95% of kids
 - Consolidation: more drugs to mop up residual blasts, including CNS prophylaxis (some drugs don't penetrate CNS well)
 - But 60 – 80% chance of relapse over next 2 – 4 years
- Bone Marrow Transplantation:
 - = Haematopoietic stem cell transplantation

- ↑Kill of leukaemic cells with ↑dose: but limited by marrow toxicity. With marrow transplantation can push dose higher (limit is organ toxicity) if cancer is responsive
- Process: patient and donor preparation, conditioning (chemo & high does radiation), stem cell infusion, neutropenic phase, post neutropenic phase
- Sources of stem cells: Self (autologous), twin (syngenic), HLA matched sibling (allogenic), HLA partial matched sibling, matched unrelated donor (MUD)
- Peritransplant mortality = 20%

Fever in a Neutropenic Patient

- Eg in patients undergoing chemotherapy
- Indicators of serious infection:
 - Signs and symptoms of infection will be reduced – can't mount an inflammatory response
 - Temperature:
 - > 38.5 C
 - > 38 for 4 hours
 - Patient feels unwell but no temperature
 - Neutropenia:
 - Neutrophils < 0.5 * 10E9/L (less than 0.2 ⇒ serious concern)
 - Neutrophils falling
 - Prolonged neutropenia (> 7 days)
- Types of infection (drives focused history)
 - Respiratory: SOB, cough
 - Skin infection
 - Mouth and teeth
 - Perianal (pain on moving bowels and wiping)
 - Pain around central line
 - Less often: bowel & UTI
- Focused exam:
 - Signs of septic shock: Pulse, BP and peripheral circulation
 - Chest: percussion and auscultation
 - Mouth: a good look around – abscesses will be sensitive to pain
 - Skin infections, especially lines
 - Quick abdominal
 - Exam perianal area – test for sensitivity to touch. Don't do PR (risk of minor trauma → bacteraemia)
- Investigations:
 - FBC
 - Blood culture (debate about whether to take it from the central line or not)
 - CXR
 - Swabs from anything that looks infected, including central line
 - Maybe CRP: ↑ in bacteraemia
- Normally don't find anything. Over half infections are low grade line infections
- If in doubt, treat empirically *now*. If infected will deteriorate quickly:
 - Gentamycin + Ticarcillin (synthetic penicillin)
 - Monotherapy (eg imipenem)
 - +/- Vancomycin (for staph line sepsis)
- Causes of infection:

	Frequency	Risk
First Fever		
Staph	+++	+
α haemolytic strep	+	++
G -ive bacilli	+	+++
Subsequent infections		
Staph	+++	+
Fungi	++	+++
Resistant G-ive	+	+++

- Subsequent fevers: longer in hospital (↑hospital acquired infection), longer on antibiotics, etc

- If fever persists:
 - Repeat the above exam and investigations – but unlikely to add anything new
 - Choices:
 - Change antibiotics
 - Consider antifungal: Amphotericin. Watch for nephrotoxicity and the patient feels awful
- Obscure fevers:
 - Central venous line infection
 - Occult sinusitis (check with CT)
 - Hepatosplenic candidiasis (check with CT → abscess → biopsy)
 - Pulmonary/disseminated aspergillus (doesn't respond to amphotericin)
 - Viral
 - Drugs
- Prevention:
 - Avoid hospitalisation
 - Strict hand washing
 - Avoid invasive procedures (beware interventionist surgeons!)
 - Care of IV devices
 - Consider prophylactic antimicrobials
- Prophylaxis
 - Bacteria: selective gut decontamination (origin of many infections is bowel flora): Ciprofloxacin (fluorinated quinolone). Arguments for and against
 - Anti-fungal: Fluconazole, Itraconazole (OK for prophylaxis, not so good as amphotericin for established infection)
 - Anti-viral: acyclovir (for HSV), ganciclovir (for CMV)
 - Anti-pneumocystis: co-trimoxazole (but beware marrow suppression) or aerolised pentamidine
- Other possible treatments:
 - Granulocyte-CSF: try to ↑ marrow production of neutrophils
 - Maybe γ -globulin infusions
 - Transfuse granulocytes: emerging area

Lymphoproliferative Disorders

Multiple Myeloma

- = A neoplastic proliferation of plasma cells, characterised by lytic lesions, bone marrow failure and homogenous serum and urinary globulin elevations

Epidemiology

- 10% of haemopoietic malignancies
- 12 – 16 new cases in Wellington each year
- Median age approx. 70 (rare under 40), male > female
- Remains incurable
- Association with lead, chemicals, agricultural work and FH of autoimmune disorders

Pathogenesis

- Monoclonal
- Arises in lymphoid follicle and disseminates to bone marrow. Plasma cells not seen in blood until terminal stage
- Stromal cells release IL6 → acts on osteoclasts to cause lytic lesions → Crush fractures in spine, nerve compression, diffuse osteoporosis, hypercalcaemia. Treat vertebral fractures with radiotherapy

Presentation

- Bone pain, pathological fracture
- Anaemia
- Amyloidosis in 10 – 15%: macroglossia, cardiomegaly, peripheral neuropathy. Diagnose with rectal/bone marrow biopsy. Stain with Congo Red
- Renal complications:
 - Presents with heavy proteinuria, also chronic renal failure – due to infiltration

- Light chain nephropathy \Rightarrow worse prognosis. Casts of free light chains \rightarrow obstruction and are directly nephrotic
- Amyloid deposition \rightarrow nephrotic syndrome
- Recurrent bacterial infections
- Rarely ‘Hyper-Viscosity Syndrome’: due to \uparrow IgM or IgG \rightarrow retinal haemorrhage

Lab Findings

- Normochromic, normocytic anaemia
- \downarrow Platelets in advanced disease
- \uparrow ESR
- \uparrow Serum uric acid
- Bone marrow: \uparrow plasma cells
- Monoclonal band on electrophoresis
- Light chains (Bence-Jones Proteins) in urine
- X-rays: multiple punched-out lytic holes in the bone, no sclerosis
- Gross: ‘currant jelly’ – soft, red lesion
- Micro: resemble plasma cells but variability in cell shape, prominent nucleoli, multinucleation
- Differential: chronic osteomyelitis – but will have granulation tissue with at least a sprinkling of other inflammatory cells

Treatment

- General treatment:
 - Over 65: Melphalan/prednisone
 - Younger: Vincristine, Adriamycin, Dexamethasone
- Emergency treatment:
 - Hypercalcaemia: pamidronate – coats bone surface to stop osteoclast reabsorption
 - Anaemia: transfusions
 - Hyperviscosity: plasmapheresis
 - Renal failure: dialysis

Prognosis

- Median survival 3 years
- Some develop AML or MDS
- Transplant (auto) extend survival
- Allo-transplants may cure a select few

Aside: Causes of Paraproteinaemia

- Benign monoclonal gammopathy: level < 30 g/L (low cf. MM), no light chains in urine. Other Ig’s normal (cf. suppressed in MM). 15-20% go onto MM but may take 10 – 20 years
- Lymphoma or CLL
- Multiple myeloma
- Waldenstrom’s Macroglobulinaemia: monoclonal proliferation of B cell lineage (half way between lymphocytes & plasma cell). Slowly progressive lymphoma. Monoclonal IgM paraprotein. Present with big glands/liver/spleen – no bone lesions

Aside: Conditions associated with Monoclonal proteins

- Associated with uncontrolled proliferation:
 - Multiple myeloma
 - Solitary plasmacytoma
 - Waldenstrom’s macroglobulinaemia
 - Lymphoma
 - Lymphocytic leukaemia
 - Heavy chain disease
 - Primary amyloidosis
- Associated with controlled proliferation:
 - MGUS: difficult to distinguish from malignancy, especially in early stages. Tend towards malignancy if:
 - Serial M band levels are increasing
 - Bone lesions

- IgG > 30 g/l or IgA > 20 g/l
- Serum or urine light chains present
- Normal Igs decreased
- Marrow plasma cells > 10%
- Renal failure
- Hypercalcaemia
- Anaemia
- Chronic infections
- Non-lymphoid malignancy
- Connective tissue disorders
- Transient (virus, drug reaction)
- Peripheral neuropathy
- Transplants

Chronic Lymphocytic Leukaemia

- Monoclonal proliferation of mature B cells (CD 19 & 20+). Being mature, will have surface expression of immunoglobulins

Epidemiology

- Commonest leukaemia: 25%.
- Primarily elderly
- Male = 2 * Female

Clinical Features

- Asymptomatic (40 – 70%)
- Insidious, maybe weight loss, fatigue
- Symmetrical enlargement of superficial lymph nodes (50%)
- Splenomegaly and hepatomegaly
- ↓Platelets → bruising
- Defects in CMI and ↓Ig → infections: Herpes Zoster (shingles), fungal, bacterial, viral. Death usually due to infection

Diagnostic Criteria

- Blood lymphocytes > 5 * 10E9/L
- Lymphocytes are B cells (CD19, 20 and 24)
- Marrow lymphocytosis > 30%

Differential Diagnosis

- Reactive lymphocytosis: EBV, CMV, HZV, Toxoplasmosis, Brucellosis, Tb, Viral
- Other B cell tumours:
 - Prolymphocytic anaemia
 - Hairy cell leukaemia
 - Splenic lymphoma with villous lymphocytes
 - Mantle cell lymphoma
 - Follicular lymphoma

Lab

- 20% diagnosed on routine blood test
- Lymphocytosis: > 5 * 10E9/L, but may be 30 to 300. Small lymphocytes and smudge cells common. (cytoplasm fragile – breaks easily)
- Normal looking lymphocyte: small, little/no cytoplasm
- Anaemia in later stages due to marrow replacement and ↓survival. 15% have Combes positive haemolytic anaemia
- Marrow: lymphocytic replacement
- 10% have haemolytic anaemia

Treatment

- Only if nodes painful: Prednisone (1 mg/kg), Chlorambucil, fludarabine. Side effects of prednisone: weight gain, hyperexia, mood changes (euphoria → depression), candidiasis, polyuria (secondary to glucose intolerance), dyspepsia

- Supportive treatment for infections, and radiotherapy for deposits causing pressure symptoms
- Little impact on viscosity (its mainly RBCs and blasts that affect that)
- Doesn't convert to Acute Lymphatic Leukaemia
- Median survival from diagnosis: 4 years. But 15% live for 15 years with no treatment

Complications Include

- Infections, secondary to hypogammaglobulinaemia, neutropenia, drugs (immunosuppressive)
- Cardiac dysfunction: secondary to chemo toxicity, etc
- DVT: hypercoagulable

Lymphoma

- Malignant lymphoma = Clonal proliferation of lymphocytes arising in lymph nodes (or other lymphoid tissue). Minor exceptions – can get them in spleen, gut, etc
- Differentiating lymphoma from leukaemia: was its *origin* in the bone marrow or lymph nodes?
- Clinical features:
 - Painless lymphadenopathy: non-tender, rubbery
 - Hepatosplenomegaly
 - Systemic symptoms: fever, night sweats, weight loss, tiredness
 - Involvement of other areas: skin, CNS, GI, salivary glands
 - If bone involvement (fairly rare) then preference for bones with red marrow, and may present with bone pain
- Diagnosis: excision biopsy (not FNA). Special lab procedures, stains etc. Warn the lab it's coming
- Classification:
 - Hodgkin's vs non-Hodgkin's: histological diagnosis only. No clinical difference. Hodgkin's responds better in general. In general, Hodgkin's spreads node to node, non-Hodgkin's spreads to any node in the body
 - Low (indolent) vs intermediate vs high (aggressive) grade
 - Staging: Ann Arbor Staging System (Ann Arbor is a place in the USA):
 - 1: one lymph node area only
 - 2: 2 or more lymph node areas on the same side of diaphragm
 - 3: 2 or more lymph node areas on different sides of the diaphragm
 - 4: disease in liver, bone marrow or other extra-nodal sites
 - Symptom status: A = absence of fevers, sweats, weight loss. B = one of unexplained fever > 38.5 C, weight loss > 10 % in preceding 6 months, drenching night sweats [Unusual to include symptom status in cancer staging]
 - Staging investigations: CT of neck, chest and abdomen. Bone marrow. FBC, LFTs, ESR
 - Compared with leukaemia: if it's in your bone marrow it's everywhere
- Survival:
 - Hodgkin's Disease:

	5-year survival (%)	10-year survival (%)
Stage I	90	73
Stage II	87	69
Stage III	71	54
Stage IV	45	< 37

- Non-Hodgkin's Lymphoma:

5-year survival (%)		
Favourable histology	Localised	61 – 90
	Widespread	50 – 70
Unfavourable histology	Localised	76 – 100
	Widespread	80 - 85

- Treatment:
 - Radiology if localised (main side effect is tiredness)
 - Chemo if disseminated
 - Possible bone marrow transplant if chemo fails (permits more toxic dose of chemo)
 - If treatment fails then gradual progression

Hairy Cell Leukaemia

- Indolent B cell neoplasm.
- Males to female = 5:1. Median onset age 50
- Splenomegaly
- Wispy changes to cytoplasm of B cell
- Purine analogues → 80% remission

Data Interpretation: Leukaemia & Lymphoproliferative disorders

- Normal count but atypical lymphocytes ⇒ viral infection. Check glands/spleen. Test for EBV, CMV, or HIV. Ensure time to seroconvert
- If only a few blasts in blood (e.g. 1%) and some nucleated red cells ⇒ not acute (blasts not dominant) but marrow under stress ⇒ chronic

Immunodeficiency

Immunology

	Natural	Specific
Circulating molecules	Complement	Antibodies
Cells	Phagocytes: macrophages, neutrophils, NK cells	Lymphocytes

- Natural immunity:
 - Integrity of skin & mucosal surfaces
 - Clearance of surfaces (eg cilia)
 - Antiseptic chemicals (eg lysozymes in tears)
- Specific immunity:
 - Has memory and specificity
 - Turns on, then off
 - Humoral (antibodies): generally extracellular bacteria. First exposure, mainly IgM. Subsequent exposures, more antibody, and mainly IgG
 - CMI/T-cells: intracellular
- The categories of things that go wrong:
 - Immune deficiency: can't fight an external agent
 - Auto-immune: inappropriate reaction against an internal antigen
 - Allergy: inappropriate reaction against an external antigen
- Causes of immune deficiency:
 - Autoimmune Disease
 - Vitamin/mineral deficiency: B12/Zinc
 - Genetic patterns: autosomal recessive
 - Metabolic deficiency e.g. Adenosine deaminase deficiency
 - Arrest in embryogenesis

Primary Immunodeficiency

- Most single gene disorders: range of effects e.g. antibody or complement deficiencies
- Clinical features:
 - Highly suspicious: chronic, recurrent or unusual infections, incomplete response to treatment
 - Moderately suspicious: skin rash (eczema, candida), diarrhoea, growth failure, recurrent abscesses, hepatosplenomegaly
- Different infections associated with different disorders
 - ↓Antibodies: sino/pulmonary/gut problems
 - ↓CMI: multisystem (e.g. CMV), pulmonary (PCP, aspergillus, candida), viruses (e.g. Herpes)
 - Phagocytic problems: s. aureus
 - ↓Complement: recurrent neisserial infection
- Symptoms depend on where in the lineage the defect is:
 - Stem cell: eg SCID
 - Pre-B cell: X Linked Agammaglobulinaemia
 - Maturation Defect: eg can't switch from IgM to IgG

Group 1 – Combined Variable Immunodeficiencies (CVID)

- Prevalence 1 in 20 – 50,000
- Symptomatic at 15 – 35 years (but long diagnostic delay)
- Recurrent pyogenic problems/autoimmune features/respiratory infections
- GI infections: giardia, campylobacter, HCV
- Normal B cells: but defect in maturation – no plasma cells
- Treatment: iv Ig (e.g. Intragam), prophylactic antibiotics
- E.g. x-linked SCID (Severe Combined Immunodeficiency), Adenosine deaminase (ADA) deficiency

Group 2 – Antibody deficiencies

- Diagnosis of primary antibody deficiencies:
 - Serum Ig's
 - Quantitative measurement essential (electrophoresis insensitive)
 - Severe hypogammaglobulinaemia: serum IgG level below 3 g/L in adults
 - Response to vaccination (important test)
 - Tetanus and Pneumo-Vax
 - Do baseline, vaccinate, expect 4 times ↑ at 4 weeks
 - IgG subclass concentrations: interpretation difficult. Based on lymphocyte count. E.g. if lymphocytes normal then primary, if low lymphocytes then ?SCID
 - Lymphocyte Subsets:
 - Absence of B cells in Bruton's
 - CVID: up to 30 % have T cell reductions
 - CLL - ↑CD5+ B cells
- IgA Deficiency (most common genetic deficiency)
 - Approx 1 in 700
 - → Respiratory & GI infections
 - Risk of anaphylaxis with blood products due to reaction to exogenous IgA
 - Don't treat with Ig
 - Runs in families with CVID
 - Can be associated with:
 - IgG subclass abnormalities
 - Impaired responses to vaccination

Group 3 – Immunodeficiency associated with other defects

Group 4 – Complement deficiencies

- Opsonisation: attachment of C3 to immune complexes
- ↓C3 → pyogenic infections due to ↓ lysis

Group 5 – defects of phagocytic number or function

- E.g. severe congenital neutropenia, chronic granulomatous disease, IFN gamma receptor deficiency
- Can test for chemotaxis, adherence and phagocytic function
- Management: specific antibodies, G-CSF in neutropenia, etc

Secondary Immunodeficiency (Acquired)

Splenectomy

- RR of fatal infection ↑ by 200 times: e.g. meningitis, bacteraemia and pneumonia → OPSI (Overwhelming Post Splenectomy Infection)
- Biggest problem is encapsulated bacteria plus malaria and salmonella
- Treat with vaccination (e.g. for pneumococcal, negligent if you don't, always record in notes) + prophylactic antibiotics
- Aggressively investigate any post splenectomy patient with infection

Diabetes

- ↓Function of neutrophils & macrophages
- Staph skin diseases common
- Compounded by ketoacidosis

AIDS

- The virus: RNA virus with reverse transcriptase. Has p24 nuclear antigen. Attacks CD4+ T cells.
- Transmission: sex (\uparrow risk in receptive intercourse – male to male most significant, also in other STDs), blood and maternal transmission (\downarrow risk with AZT)
- 1 % of Europeans lack CXR-5 receptor: if homozygous then resistant
- Signs & Symptoms:
 - \uparrow Temperature, wasting (chronic ill health)
 - Rashes: eg shingles, HSV (cold sores), candidiasis, may be drug response (heightened sensitivity to drug responses)
 - Lymph nodes
 - Signs of high risk behaviour: Injection marks, other STD
 - Mouth: infections, Kaposi's Sarcoma (re-purple vascular non-tender tumours – mainly on skin)
 - Chronic cough common
 - Hepatosplenomegaly (infections, lymphoma)
 - Neuropathies: eg due to intracranial lesion (eg lymphoma), peripheral sensory neuropathies
 - Fundi: cotton wool spots, scars (eg due to toxoplasmosis, CMV)
- Early disease:
 - Seroconversion illness: in 50 – 90% of infected people. May include macular rash
 - Debate about usefulness of early treatment
 - Good evidence of value of prophylactic treatment (e.g. following needle stick)
- Screening:
 - 3 weeks before positive after infection
 - Elisa for HIV-1 and HIV-2 antibodies
 - False positive tests: 4/1000
- Confirmatory diagnosis: Western Blot
 - Can take up to 3 months to get Western Blot Positive
 - Can give indeterminate, weak positive or strong positive (3 bands)
- Course: measure based on viral load and CD4 count
 - Acute illness: 4 – 8 weeks
 - Asymptomatic: 2 – 12 years
 - Symptomatic: 2+ years. AIDS defining illness:
 - PCP infection (treat with co-trimoxazole): can \rightarrow pneumothorax
 - Cryptococcus infection: mild headaches: lumbar puncture. Indian ink stain positive
 - Kaposi's sarcoma: can present anywhere
 - Psychological: HIV related, secondary illness related, or depression
- Viral Load:
 - High T cell turnover: Virus replicates in 1½ days. Infected cell lasts 2.2 days
 - HIV in sanctuary sites: e.g. brain – hard to treat
 - Measure through PCR of viral RNA: good indicator of progression. If viral load high, treat now
- Immune depletion: Based on CD4+ count:
 - > 500
 - 200 – 500: Tb, herpes
 - < 200
- Subgroups of illness:
 - Constitutional: fever, diarrhoea, weight loss
 - Neurological: dementia, neuropathy, cognitive
 - Opportunistic infections: candida, PCP, toxoplasmosis, CMV, MAC, Tb
 - Malignancies: Kaposi's sarcoma, non-Hodgkin's lymphoma
- Drug Treatment:
 - Combination of drugs that inhibit various points of viral replication
 - Can improve CD4+ count from very low (e.g. 50) to e.g. 500-600
 - Side-effects: non-specific rashes, 'buffalo hump' – abnormal fat distribution
- Leading cause of death: Respiratory infection

Testing for HIV

- Guidelines for HIV pre-test counselling:
 - What the test for HIV antibodies means: not a test for AIDS
 - Significance of negative test (Window period)

- Significance of positive test: medical implications (prognosis & treatment), social implications (coping, support, relationships, who needs to know, possible discrimination), notification requirements (HIV not notifiable, patient can use alias), implications for insurance
- Safeguards to preserve confidentiality
- Future preventative aspects: safer sex and IVDU
- How results are obtained
- Any costs
- Guidelines for post test counselling:
 - Explanation of test results
 - If negative: 3-month window period – especially if recent high risk behaviour. Future prevention
 - If positive: repeat, confirmatory test organised, arrangement for counselling, support and specialist assessment

Other Causes of Secondary Immunodeficiency

- Malignancy
- Drugs e.g. steroids, cyclosporin, cytotoxics
- Nutritional Deficiency
- Post-viral
- Post-transfusion
- Alcoholism
- Chronic renal disease

Allergy and Hypersensitivity Disorders

Hypersensitivity

- A lay term
 - Stimuli that don't cause symptoms amongst general population
 - Usually reaction of body surfaces (eyes, airways) to environmental factors
- Immunological Hypersensitivity Types:

		Problem With	Mechanisms
I	Immediate Hypersensitivity	IgE	Allergen reacts with antibody on the surface of mast cells or basophils → mediator (eg histamine) release
II	Cytotoxic / Antibody mediated	IgM, IgG	IgG or IgM against antigens on one's own tissues. Antibody binding → complement activation → ↑WBC → tissue injury. Eg Goodpasture's Syndrome (Ab against glomerular basement membrane), haemolytic disease of the newborn.
III	Immune Complex Mediated	Antigens + Ig	Antibody complexes are not cleared from the circulation and fix in capillary beds → ↑WBCs → tissue damage. Eg serum sickness (foreign proteins and drugs – eg Cefaclor [cefaclor] – urticaria (hives, welts) 1–7 days later) and some glomerulonephritis
IV	Delayed Hypersensitivity / T cell mediated	CD4/8	TcR (T Cell receptor) binds to tissue antigens → clonal expansion and inflammatory cytokine release. Eg contact dermatitis, tuberculin sensitivity in Tb.

- Autoimmune disease can be any one of types II, III or IV
- Hyperreactivity = ↑ sensitivity to non-specific stimuli (= irritants), eg cold, perfumes, etc

Allergy

- Cross references:
 - See also Food Allergy, page 647
 - See also Atopic Eczema, page 319
 - See also Allergic Rhinitis, page 63

- See also Drug Allergy, page 530
 - = Immunologic reaction to common substances which are harmless to most people
 - Previous exposure → antibodies or specific lymphocytes against these substances
 - Types:
 - Atopy:
 - Predisposition to produce IgE antibodies to common environmental substances (also called immediate or Type 1 hypersensitivity).
 - Order of incidence:
- | | Peak in years |
|-------------------------------|---------------|
| Eczema | 1 – 2 |
| Food allergy (eg milk, eggs) | 2 – 3 |
| Asthma | 10 |
| Seasonal Rhinitis (hay fever) | 20 + |
- Adults aged 20 – 44 in New Zealand: Asthma 15%, hay-fever 35%, Maori more symptomatic
 - Mediators lead to vasodilation, vascular leakage (swelling), smooth muscle spasm (eg respiratory).
 - Similar symptoms can occur from non-allergic hypersensitivity => non-atopic
 - Contact Allergies: direct skin contact with nickel, chrome, rubber. Due to lymphocyte (delayed-type hypersensitivity, type IV) not IgE antibodies
 - Allergic Alveolitis → lung inflammation. Eg farmer's lung, pigeon fancier's lung. Due to lymphocytes and IgG (not IgE)
 - Risk factors:
 - Allergy predominates in young adults and children: while non-specific hypersensitivity is more common later in life
 - Genetic Factors: One parent → doubled risk of child having atopic disease. Both parents → 4 times risk
 - Early childhood factors important in subsequent development of allergic disease:
 - High house dust mite/cat/pollen exposure in early months → ↑risk
 - Exposure to tobacco smoke in utero/infancy → ↑risk
 - Early life infections → ↓risk: ?improved shift from TH2 environment of uterus to non-allergic TH1 immune responses which dominate in most infections (especially intracellular pathogens)
 - First born children at greater risk
 - The workplace is a major source of allergen exposure
 - Bee sting allergy:
 - Don't have to have atopic history
 - If anaphylaxis as a child, 1 in 6 chance next time. For adult, 60% chance next time
 - Carry adrenaline until desensitisation (serial antigen shots → 95% effective)
 - Anaphylaxis: give 0.5 mL of 1:1000 adrenaline **IM** if in community setting (iv in hospital if you can give slow infusion). IM gives good diffusion, safer, effective and fewer problems with cardiac vasoconstriction cf bolus
 - For treatment of Anaphylaxis see Severe Anaphylaxis, page 483

Diagnosis

- History: do symptoms occur in particular environments, particular times or seasons, what are dominant symptoms (eg sneezing/itching more likely to be allergy than chronic nasal blockage)

Skin prick tests

- Useful for atopic allergies: especially of the mucous membranes
- Use standard panel of allergen extracts (eg grass pollen, house dust mite, cat dander, etc)
- Read wheal and flare reaction 10 – 15 minutes later
- Safe, accurate and cheap
- If they have had an anaphylactic reaction → test in a hospital setting. If very highly sensitive → systemic reaction. If anaphylactic reaction, test tryptase (elevated for 1 – 6 hours)
- Skin prick tests will be negative in hypersensitivity that is not IgE mediated
- Pathophysiology:
 - Allergen + specific IgE (attached to mast cells) → mast cell activation → degranulation → histamine and tryptase release + newly generated mediators (arachidonic acid metabolites eg leukotrienes and PGs) → local & systemic effects. Eosinophils may also produce mediators of inflammation

- In the sensitisation process antigen presenting cells (dendritic cells, macrophages) present allergen fragments (epitopes) to T helper cells using MHC Class II. Mainly Th2 cells involved in inducing allergic disease → IL4, IL5, IL3 → IgE production, eosinophil growth and differentiation and mast cell growth

Lab tests

- Tests for IgE antibodies (eg RAST tests) are available for certain allergens. But also rises for parasites – where in the world were they raised – this could be a cause
- Indicate immune sensitisation only. Allergy requires symptoms following exposure
- Expensive and less accurate than skin tests, but useful if skin tests not possible, history of anaphylaxis

Challenge tests

- Mainly in research setting
- Food allergy: can do double blind, placebo-controlled food challenge. In small kids, removing food allergens from diet will improve severe eczema – but not in adults
- Inhalation of cold air, histamine or exercise may be useful in assessing bronchial hyperreactivity in asthma

Contact Allergy

- Affect whole skin and are usually life long
- Diagnosed using patch testing on back for 48 hours. Difficult to distinguish between allergic and irritant reactions

Diseases caused by Antibodies

Antibodies against tissue antigens

- Cause disease specific for that cell/tissue
- Usually auto-antibodies: but may be a foreign antigen that is immunologically cross-reactive with a component of self-tissues
- Usually IgG or IgM
- Antibodies may be specific for cellular structures: eg receptors. May lead to interference in function, eg myasthenia gravis, Graves disease

Immune complexes formed from a soluble antigen and specific antibody

- Formed in the circulation, deposit typically in arteries, glomeruli, synovia
- Leads to local leucocyte activation and tissue injury
- Antigens can be foreign or self antigens, antibodies are usually IgG or IgM

-
- References:
 - Mainly Dr Lisa Judd's notes in GP, Paediatrics and Musculo-skeletal
 - Prof Delahunt's Pathology notes
 - Dr Stanley's Paediatric eczema notes

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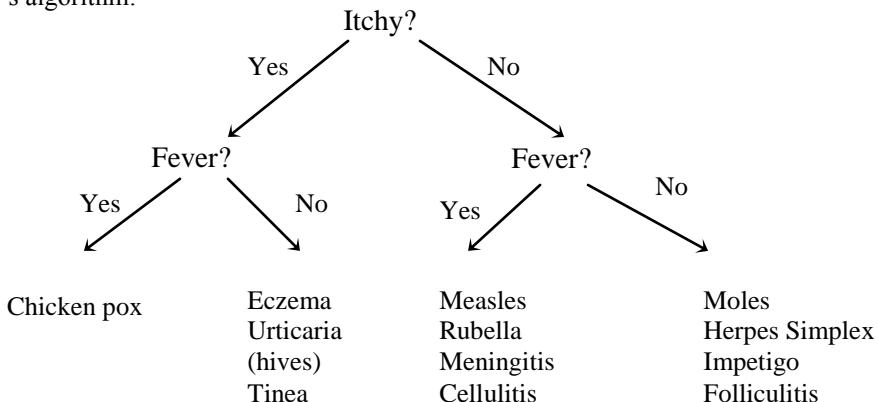
Dermatology Glossary

- Annular lesion - ring shaped
- Erythema: dilation of blood vessels – colour goes away if pressed (blanching)
- Macule: an alteration in colour (e.g. macular erythema)
- Papule: a small lump, less than 0.5 cm in diameter
- Nodule: lump bigger than 0.5 cm
- Erythematous-squamous: red and scaly
- Plaque: elevated (maybe only very slightly) area of skin > 2 cm. Altered texture
- Vesicles and bullae = fluid within or beneath epidermis (blister). Vesicles < 0.5 cm, bullae > 0.5 cm.
Can have both. E.g. vesicular-bullae eruption from a plant allergy
- Pustule: accumulation of pus (can be just inflammatory not infectious, e.g. psoriasis)
- Cellulitis: inflammation of deep dermis and subcutaneous tissue
- Ulcer: loss of dermis and epidermis
- Scale: at edge of inflammatory lesion, can be fine, large, dark, silvery (psoriasis)
- Scar: fibrous tissue due to healing. Atrophic scar is thin and wrinkled. Hypertrophic scar is elevated
- Poikiloderma: cutaneous pigmentation, atrophy and telangiectasia
- Comedo – pl. comedones: a plug of keratin and sebum in a dilated pilosebaceous orifice. Closed comedo = blackhead, open comedo = whitehead
- Cyst: any closed cavity with a membranous lining containing fluid
- Petechiae – pl., petechiae: a haemorrhagic spot 1 – 2 mm diameter
- Purpura: haemorrhagic spot > 2 mm. Pressing down doesn't blanch – red cells are extravascular → ?vessel damage. If purpura are palpable ⇒ vasculitis
- Ecchymoses: bruises – larger extravasations of blood
- Telangiectases: permanently dilated small vessels
- Guttate: a profusion of small macules or plaques
- Serpiginous: a linear eruption which is S shaped or snake like (e.g. larva migrans – a worm)
- Dermatitis: usually means eczema
- Structure of skin:
 - Epidermis:
 - Stratum corneum
 - Stratum lucidum
 - Stratum granulosum
 - Stratum spinosum
 - Stratum germinativum (base of epidermis)
 - Dermis:
 - Papillary dermis
 - Reticular dermis
 - Subcutaneous tissue
- Basic terms: Non-specific reactive changes
 - Hyperkeratosis: thickening of the stratum corneum. Eg due to trauma (eg the lump where you hold a pen)
 - Parakeratosis: Nuclei are seen in the stratum corneum (would normally have died off, eg psoriasis)
 - Acanthosis: thickening of the epidermis, eg due to irritation

Diagnosis

- Where is it:
 - Psoriasis: likes scalp and extensor elbows/knees
 - Atopic eczema: likes flexor elbows and knees
 - Nose & cheeks: lupus, especially if it leaves a pigment behind
- Does it itch?
 - Atopic eczema (if it doesn't itch it's not eczema)
 - Chicken pox
 - Urticaria/allergic reactions
 - Contact dermatitis
 - Scabies

- Insect bites
- Fungal infections
- Dermatitis herpetiformis
- Pityriasis Rosea
- Idiot's algorithm:



Skin Infections

Bacterial infections of skin and soft tissue

Impetigo (School Sores)

- = Superficial infection involving the epidermis
- Most common in children during summer months
- Non-bullous impetigo:
 - = Streptococcal impetigo
 - Vesicles on erythematous base → pustules (highly contagious) → yellow-brown scabs (CRUSTY), associated with regional lymphadenopathy
 - Ecthyma is deeper version – cut out edge
 - Commonly result of skin break such as insect bites or chicken pox. Especially if overcrowding and warmer climates
 - Goes for limbs and face
 - Fever uncommon. Check lymph nodes
 - Caused by Streptococcus Pyogenes with or without co-infection with Staphylococcus Aureus (can → Scalded Skin Syndrome, see page 315)
 - Commonest cause of post-strep glomerulonephritis
- Bullous impetigo:
 - Due to Staph aureus of phage II (usually type 71)
 - Usually younger children
 - Lesions: begin as vesicles – turn into flaccid bullae in response to toxins. Following rupture of the bullae, a moist red surface remains and varnish like crust appears
- Neonatal Impetigo: Staph Aureus. Can spread to deeper tissues, umbilicus, bone and joints. If only one site, antiseptic bath once a day. If > 1 site then systemic antibiotics
- Treatment:
 - To relieve symptoms, stop new lesions, prevent complications (e.g. cellulitis, acute glomerulonephritis), and stop spread to others
 - Flucloxacillin, dicloxacillin, a cephalosporin, erythromycin or clindamycin are all effective
 - If MRSA: usually susceptible to co-trimoxazole (although not so good against S Pyogenes). Resistance to fusidic acid is also growing
 - Resistance is growing to topical agents (e.g. Mupirocin)

Scalded Skin Syndrome

- Due to staph aureus toxin (may be distant site)
- Skin peels off with little pressure – skin looks abnormal – damage from within
- Commonest in infancy
- Treatment: flucloxacillin plus burn treatment (including fluid balance)

Folliculitis

- Pyoderma located within the hair follicle
- Usually caused by *S aureus*
- Responds well to topical antibacterial measures

Furuncle

- = A ‘boil’
- A deep inflammatory nodule
- In skin areas subject to friction and perspiration and containing hair follicles
- Often drain spontaneously, especially with moist heat
- If recurrent, then ?nasal carriage of *S aureus*. Treat with topical intranasal mupirocin or systemic rifampicin
- May progress to a carbuncle: more extensive involving subcutaneous fat. If surrounding cellulitis or if on face then need iv antibiotics

Cellulitis and Erysipelas

- Infection of subcutaneous layer by *Strep Pyogenes*
- Symptoms: inflammation, warmth, erythema, pain, fever
- Can → sepsis, bullae and small abscesses
- Also erythema around anus with puss and blood in stool
- May desquamate
- Impaired lymphatic drainage predisposes to recurrent cellulitis (e.g. pelvic, joint, breast surgery)
- Erysipelas is a distinctive superficial cellulitis, primarily involves dermis. Raised and well demarcated. Prominent lymphatic involvement. May → chills, fever and malaise
- Treatment: *S Pyogenes* still very susceptible to penicillin

Diabetic Foot infections

- Due to neuropathy, ischaemia, and infection
- Causes: often *S aureus*, also coagulase negative staphylococci and streptococci
- Often nasal carriage of *S aureus*
- Treatment: anti-staphylococcal agents. IV treatment if deep tissues or bone involvement

Deep Tissue Infections

- Necrotising Fasciitis: See *Streptococcus Pyogenes* (Group A, β Haemolytic), page 500
- Superficial necrotising cellulitis or streptococcal gangrene (rare)
- Gas Gangrene (Clostridial myonecrosis): rapidly progressive and life threatening infection of muscle due to *Clostridium Perfringens*

Scarlet Fever

- See *Streptococcus Pyogenes* (Group A, β Haemolytic), page 500

Lymphadenitis

- May require drainage. Distinguish from lymphadenopathy
- Usually *Staph aureus*, also TB
- See Cervical Lumps, page 648

Toxic Shock Syndrome

- See *Streptococcus Pyogenes* (Group A, β Haemolytic), page 500
- Desquamation a week later characteristic

Dog Bites

- Clean carefully (may need local anaesthetic)
- Treat with broad-spectrum antibiotic. Amoxycillin/clavulanate. NNT = 14. So limit to high risk of infection only. Consider anaerobe cover (eg metronidazole)
- Screen for post-traumatic stress disorder afterwards
- Report the dog

Lyme Disease

- Tick borne spirochete (*Borrelia burgdorferi*)
- Gives erythema migrans, headache, fever, myalgia, fatigue

- Leads later to widespread systemic manifestations
- Discovered in Connecticut, USA. Not in NZ

Fungal Infections/Dermatophytosis

- = Tinea
- Fungal infections of animal (zoophilic) origin: These include “ringworm” (which causes a scaling macule – not a ring – and there is no worm!). Usually in children, for example from cows, dogs, cats or mice

Clinical Description

- Fungal infections usually itch. Have a raised scaling margin that extends outwards
- There are several classical presentations:
 - Tinea Cruris: in the groin. Mainly affects men. Sharp margin. On thighs or buttocks may get follicular pustules. If feet involvement as well then systemic treatment, otherwise topical
 - Tinea Capitis: Scalp. Invasion of hair shaft. Causes alopecia. Usually *M Canis*. Usually children aged 3 – 7, nearly always cervical occipital lymphadenopathy. Needs systemic treatment (topical doesn't penetrate hair shaft).
 - Athlete's Foot/Tinea pedis: on the feet (usually lateral toe clefts – compared with eczema which in medial toe clefts). Increased sweating predisposes to fungal infection. It can be spread to the sole with a powdery scale. To hands by itching, where it presents with a dry, hot rash on one palm, with well defined lesions with a scaling edge
 - Tinea Corpus: on the trunk. Presents with an erythema and itching, and a well defined, scaling edge. May not itch
 - Tinea manuum: Hand. Almost always a pre-existing foot infection.
 - Fungal infection of the nail (Onychomycosis): occur mainly in adults, usually in their toenails (fingernails uncommon, ?psoriasis), and especially following trauma. The nails become thickened, yellow, and crumble, usually asymmetrically. The changes occur distally, and move back to the nail fold (compared with psoriasis, which is symmetrical and moves distally from the nail fold)
 - Tinea Incognito: Fungal infection treated with steroids. Stops inflammation but fungus slowly spreads → follicular pustules etc.
- Tinea Versicolor:
 - Infection due to a commensal yeast *Malassezia Furfur* (= *pityrosporum ovale*. Not a fungus). In young adults, causes hypo- or hyper-pigmented macules with powdery scale, on upper trunk, upper arms and neck. Slightly itchy
 - Differential diagnoses:
 - Vitiligo: but pure white lesion (amelanotic), no scaling
 - Pityriasis alba: Usually children and on the face. Tinea Versicolor rare in children
 - Treatment: Imidazole cream, sporanox, selsun shampoo

Diagnosis

- Consider in any patient where isolated, itching, dry and scaling lesions occur for no reason (e.g. no history of eczema). Fungal lesions are usually asymmetric. Clippings or scrapings can be sent for culture

Pathogenesis

- Common: *Microsporum Canis* (from cats, fluoresce under Wood's light), *Trichophyton rubrum*, and *Trichophyton mentagrophytes*
- Less common: *Trichophyton tonsurans*, *Epidermophyton floccosum*, *Trichophyton erinacei*
- Fungi consist of thread-like hyphae that invade keratin (yeasts do not have hyphae). Vegetative spores (conidia) develop in culture. When immune response is impaired, superficial infections may invade deeper tissues

Management

- Topical Treatment: imidazole preparations, such as clotrimazole and miconazole. Dusting preparations are also available. Terbinafine is available as a cream
- Systemic Treatment: Diagnosis should be confirmed before commencing treatment. Terbinafine (250mg, once daily PO) for 2 to 6 weeks for skin infections and 3 months for fingernail infections, 6 months for toe nail infections. (Pregnancy and lactation are relative contraindications). Can take itraconazole 1 week per month for 3 months (200 mg bd) → ↓ side effects. Takes 12 – 18 months to grow a new nail. Given length of treatment, confirm with nail scraping for culture first.

Viral Infections

Molluscum Contagiosum

- Viral infection with pox virus
- Small solid papules with umbilication in middle. Stay fairly localised
- If you squeeze them then virus released (ie infective)
- Histology: acanthosis and molluscum bodies
- Disappear in under 9 – 12 months. Treat if severe

Verrucae (Warts)

- Papova virus: **Papillary lesion + polyoma** (lots of them) + **vacuolation** of cells containing the virus
- Locations:
 - Verruca vulgaris
 - Verruca plana: flat, eg on face
 - Verruca plantaris: on feet, can be painful
 - Verruca palmaris: on hands, can be painful
 - Condyloma accuminatum: Genital. Rarely premalignant
- Histology:
 - Hyperkeratosis/parakeratosis
 - Acanthosis
 - Nuclear and cytoplasmic inclusions
 - Perinuclear vacuolation

Other Viral Illness

- See Varicella Zoster504
- See Herpes Simplex Virus (HSV), page 503
- See Common Paediatric Viruses, page 617

Other Infections

Paronychia

- Loss of cuticle (due to eczema, wet work, etc) allows growth of organisms beneath the proximal nail fold → inflammation and nail dystrophy. Acute usually staph, chronic usually candida
- Differential:
 - Onychomycosis
 - Lupus, psoriasis, chilblains
- Treatment: avoid wet work, treat eczema, dying agent, systemic antibiotic if bacterial

Pitted Keratolysis

- Small craters in the sole of the foot. Asymptomatic. Foot odour
- Variously attributed to Corynebacteria, Dermatophilus, Micrococcus
- Treatment: keep feet dry, topical erythromycin, systemic tetracyclines

Pityriasis Rosea

- Usually 10 – 35. Starts with herald patch (larger than later lesions). After 5- 15 days general eruption begins. Oval, dull pink, with marginal scale. Itch varies. On trunk, rarely on face
- Was thought to be viral, but erythromycin effective
- Fades after 3 – 6 weeks
- Differential: eczema, psoriasis, seborrheic dermatitis, tinea versicolor

Candidiasis

- Yeast infection
- Common in infants – either mouth (esp inside cheeks) and in nappy area, maybe on hands if sucked. More common in damp areas. Need to treat Mum's nipple as well.
- Lesions whitish with satellite lesions characteristic
- Also with oral/inhaled steroids or broad spectrum antibiotics
- Systemic spread in immuno-compromised is nasty
- Treatment: see Antifungals, page 515

Scabies

- Irritation from hypersensitivity after 4 weeks of scabies mite burrowing
- Papular vesicular lesions

*Headlice **

- The insect: 2 – 3 mm long, breeds all year round. They live in the scalp and suck blood for food 5 or 6 times a day. They are only transmitted through close head contact. They don't come off with swimming or washing. The eggs are a similar colour to scalp skin. The empty egg shells, known as nits, are white
- Life cycle: female lice lay about 7 – 10 eggs each night, these hatch in 9 days. A louse will live for 40 days
- Where to find them: around the hairline at the back of the neck, behind the ears, on the crown
- Treat if you find a live insect or an egg within 1 cm of the scalp (hair grows 1 cm a month, so more than 1 cm from head means they're dead)
- Use special shampoo from the chemist. Leave on scalp for 5 – 10 minutes. Don't use too much water. Repeat a week later
- Don't need to wash bedclothes: lice only lay eggs on hair. Instead check kid's heads once a week
- Prevention: regular hair brushing, don't share brushes, keep clothes separate, contact tracing

Eczema

- = Dermatitis
- Formal definition: pattern of inflammatory response of the skin which can be defined histologically by the presence of a predominantly lymphohistiocytic infiltrate around the upper dermal blood vessels, associated with spongiosis (= oedema between keratinocytes) and varying degrees of acanthosis.
- Clinical features include itching, redness, weeping, scaling and clustered papulovesicles
- Endogenous forms:
 - Atopic
 - Seborrheic
 - Discoid
 - Juvenile plantar dermatosis
 - Pompholyx
 - Pityriasis Alba
- Exogenous forms:
 - Asteatotic
 - Irritant contact dermatitis
 - Allergic contact dermatitis

Atopic Eczema

- See Allergy and Hypersensitivity Disorders, page 309

Symptoms

- Onset usually 2 – 6 months
- Acutely:
 - Itchy
 - Redness, swelling, usually ill-defined border
 - Papules, vesicle, extremely large blisters, may look weepy
 - Exudates and crusting
 - Scaling
 - Can be papular
- Chronic:
 - Less vascular and exudative
 - More scaly, pigmented and thickened
 - Fissuring
 - More likely to be lichenified (epidermal thickening with exaggeration of skin markings) and develop painful fissures
 - If dark skin: post inflammation change in pigmentation
 - Pitting of nails if involved with ridging of nails

- In babies:
 - Common onset in first few weeks
 - Quite weepy/blistery
 - Around face (spares eyes and base of nose) and trunk. If extensor distribution think of contact sensitivity (eg house dust mite)
 - Can be due to antigens in breast milk
 - The itch that rashes: itchy skin is scratched and an eruption occurs – don't see rash where child can't reach
- Children, and older:
 - Bends of elbows, behind knees
 - More leathery
 - Between big toe and 2nd toe (compared with tinea between 4 and 5)
- Associated with asthma and hay fever
- Associated with food allergy – commonly cows milk but this is overstated
- Atopic skin has lower threshold to irritation (eg soaps) and is more prone to staph infection
- Prognosis: ½ have cleared by 12, few persist after age 30
- Increased tendency to: dry skin, urticaria, pityriasis alba, keratosis pilaris, irritant contact dermatitis, etc

Pathogenesis

- Genetic predisposition
- ?Imbalance of Th1 and Th2 cells in the thymus in favour of Th2
- ?Early childhood infections → preferential induction of Th1 type cytokines and prevent atopic sensitisation. ↓Infections → greater risk of atopy
- Inversely proportional to the number of older siblings (marker of exposure to infection)
- Atopy does not equal allergy:
 - Level of IgE, which may be elevated, doesn't correlate to severity
 - Up to 50% of children with eczema do not have +ive skin prick tests (especially if mild eczema and no asthma)
 - Skin prick tests for histamine release (type 1 reaction) may be positive but the person may have not reaction when exposed to that allergen
 - Rast test looks for antigen specific IgE
 - Type 1: normally asthma, rhinitis, urticaria, not usually eczema
 - Patch testing (Type 4) may be relevant to childhood eczema
 - Only 50% with severe eczema develop reactions when challenged with particular foods – most are delayed reactions
- See Allergy and Hypersensitivity Disorders, page 309

Management

- Investigations
 - Patch testing
 - Is there infection? (Yellow crusts, weepy, failure to respond to treatment) → systemic antibiotics
- Prevention:
 - Don't itch
 - Avoid aggravators:
 - Light cotton clothes, no scratchy woollens
 - Avoid excess humidity/dryness
 - Avoid local or systemic aggravators
 - Care with soaps, perfumes, solvents etc
 - Baths not shower, not too hot, pat not rub dry
 - Reduce stress
 - Control dry skin: Emollients – aqueous cream, white soft paraffin
- Medical:
 - Topical corticosteroids:
 - Reduce inflammation but doesn't treat cause
 - Use weakest possible – 1% hydrocortisone OK for most
 - At night use in conjunction with wet dressings (containing emollient)
 - Not for too long otherwise skin atrophy, striae and rebound afterwards, wrinkling, ↑vascular markings, also dynamite to viral/bacterial infections. Even worse with systemic steroids
 - Lotion for scalp, ointment for dry areas (may cause folliculitis), cream

- Strength:
 - Face and flexures: mild only
 - Scalp, palms and soles: can tolerate very potent steroids (eg betamethasone dipropionate)
 - Body and limbs: potent for short periods (a week or two), mild to moderate as maintenance
 - Systemic steroids for severe eczema, for a short time only
- Tar compounds: esp. at night to prevent itching
- Antihistamines: stop itching (more in kids and for sedative effect) and urticaria
- Antibiotics for infection
- For severe eczema: phototherapy, azathioprine, cyclosporin

Seborrhoeic Dermatitis

- Scalp, eyebrows and nasal labial folds. Cradle cap in babies whose scalp was clear at birth
- Red, greasy scale, sharply circumscribed
- In kids = another presentation of atopic. Treat the same. Differential: Infantile psoriasis
- In adults = allergy to yeast (*Pityrosporum ovale*) which arrive with grease gland activation at puberty
- Differential:
 - Psoriasis. But doesn't often affect the face
 - Discoid, and other forms of eczema
 - Pityriasis rosea (usually on trunk and not on the face)
 - Fungal infection: annular, scaling isn't greasy

Contact Dermatitis

- May be irritant or allergic or both. May co-exist with endogenous forms (eg atopic)
- Differentiate from endogenous on the basis of history, distribution and maybe allergy testing, not morphology

Contact Irritant Dermatitis

- Irritant: a substance which induces dermatitis in anyone if applied in sufficient concentration for long enough → penetrates skin and produces cellular damage
- Individuals vary in their threshold
- Heat and ↑ or ↓ hydration impair barrier function → more susceptible
- Cumulative effect of different irritants
- Irritants include: acids, alkalis, solvents, soaps, detergents, enzymes, abrasives
- Diagnosis:
 - Exposure to irritants for what length of time and frequency
 - Are sites consistent with exposure
 - Does it improve after exposure stops
 - Can contact allergy be excluded (eg have they had it since childhood ⇒ more likely to be allergy)
- Management:
 - Steroid creams, emollients
 - Reduce exposure, remove occlusion (ie sweat inside gloves → over hydration), other work

Contact Allergic Dermatitis

- Type 4 cell mediated immune reaction (see Allergy and Hypersensitivity Disorders, page 309)
- Often takes repeated exposure, so no previous symptoms may not be significant (same for type 1 reactions). Eg may have worn rubber gloves for years
- Once sensitised, further exposure to even minuscule amounts → reaction after a day or two. Takes 24 – 72 hours, compared to type 1 which takes 15 – 20 minutes
- Will involve primary sites, and maybe distant sites (eg eyes, genitals)
- Photoallergy = need exposure to allergen + UV light to cause rash. Eg sunscreens
- Common allergens: nickel (eg pierced ears), rubber additives, plants, chromate in cement, hairdressing chemicals, perfumes, ...
- Rubber glove allergy can be:
 - Type 1 due to rubber
 - Type 4 due to rubber additives
 - Contact dermatitis due to sweaty hands - ↑ risk of type 1 or 4 reaction (mediated by Langerhans cells) due to ↓ barrier function

- Diagnosis:
 - Exposure to possible allergens
 - Sites consistent with exposure, goes away when exposure stops. NB some sites resistant (scalp, soles)
 - Patch testing
- Management:
 - Steroids, emollients, etc
 - Avoid exposure

Other Eczema Related Conditions

Discoid Eczema

- Descriptive term: round or oval, well circumscribed, red, scaly, +/- vesicular (\rightarrow weepy)
- In kids: often atopic
- In Adults: often cause unknown
- Differential:
 - Ringworm: tends to be annular (worse at the edge). May have alopecia or pustules. Take scraping for culture.
 - Superficial BCC: doesn't usually itch, often a shiny surface, dots of pigment
 - Psoriasis: silvery scale, not weepy

Juvenile Plantar Dermatosis

- Fissured dermatitis of the plantar surface of the forefoot – red, glazed, cracked, symmetrical, toe clefts normal
- In children 3 – 14 years
- Usually atopic
- Treatment difficult: Urea creams, moisturisers, steroid creams. Has usually resolved by teens.

Pompholyx (dyshidrotic eczema)

- Not related to atopic eczema
- Vesicles +/- bullae on palms, soles, sides of fingers or toes
- Erythema or scaling absent. If present then just a vesicular eczema
- Heals with desquamation
- Differential: fungal infection
- Treatment: ?steroids

Pityriasis Alba

- Round/oval, hypopigmented, fine lamellar scaling, from 5 – 20 mm, commonly on face
- Usually age 3 – 16
- Associated with atopy – but may be independent
- No treatment – goes away by itself

Asteatotic Eczema

- Related to dry skin
- Usually on legs, usually diuretics, excessive washing or hypothyroidism
- Superficial fissures create a crazy paving pattern
- Treatment: soap substitute, moisturiser +/- topical steroid

Intertrigo

- Generic term for inflammatory dermatosis in skin folds (eg submammary or gentiocrural)
- May be a form of atopic or seborrhoeic dermatitis
- Can be secondarily infected with candida or staph
- Treatment:
 - Reduce friction, avoid tight clothing
 - Mild steroid, antibacterial or anti-candida cream

Angular Cheilitis

- Affects the fold of skin at the corner of the mouth. Especially in denture wearers
- May be a form of intertrigo, can be associated with atopic or seborrhoeic dermatitis

- May be infected with candida or staph, may be folate deficiency, a frequent complication of *Roaccutane* treatment

Nappy Rash

Napkin Dermatitis

- Irritant contact dermatitis caused by prolonged contact with wet nappies
- Spares the flexures
- Bacterial conversion of urine to ammonia → alkaline irritant
- Treatment: frequent changing, carefully washing, protective cream

Differential: Candidiasis

- Frequently superimposed on nappy rash
- Flexures involved + satellite lesions or superficial pustules on a background of erythema
- Treatment: antifungal cream (nystatin)

Sun Damaged Skin

- Photo-damage = Dermatoheliosis
- Damage results in:
 - Wrinkling
 - Pigmented lesions
 - Sebaceous hyperplasia (?sun damage or age)
 - Telangiectasia and purpura (thinned epidermis due to ↓basal cells + flattening out of dermo-epidermal junction → shearing forces rupture capillaries → bruising)
 - Pseudoscars
 - Benign and malignant growths
 - Skin laxity
 - Diffusely thickened skin with yellowish micropapular appearance (especially temples), etc, etc
- Damage relates to life-time dose of UV:
 - Melanoma risk determined by age 15
 - After that, ↓sun only affects BCC and SCC risk

Sunscreens

- UVA blockers: block in range 320 – 360 nm. Doesn't cause sunburn but is implicated in skin cancer as it's harder to filter out
- UVB blockers: block UV in the range 290 – 320 nm, the sunburn range, but easily filtered. SPF refers to ability to block UVB – not UVA ⇒ need broad spectrum
- Types of sunscreen:
 - Cinnamates: UVB
 - PABA: UVB (not commonly used – allergies)
 - Salicylates: UVB
 - Benzophenones: UVA
 - Camphor: UVA
 - Dibenzoylmethane: UVA (good to have in addition to a high SPF)
- Can use reflective agents (eg titanium dioxide) in addition to absorbers
- Need behaviour change as well as sunscreen

Lesions

- Solar Keratosis: See Premalignant Lesions, page 326
- Cutaneous Horn: horny outgrowth, arising from a Solar Keratosis, SCC or seborrheic keratosis. Treat according to underlying lesion
- Disseminated Superficial Actinic Porokeratosis: Caucasian. Autosomal dominant. First noticed in 40s. Up to 1 cm, slightly red/hyperpigmented on lower leg or forearms. Border has 2 parallel rows of scale
- Bowen's Disease: See Premalignant Lesions, page 326
- Chondrodermatitis: On sun damaged ears, may also be due to pressure. Commonly on helix of pinna. Painful when pressed. Differential SCC (usually large and not as painful) or BCC (pearly, not often on rim of ear). Treatment: excision including cartilage otherwise recurrence
- Lentigo: Brown macules (look like large freckles). Solitary, multiple or generalised. May be part of a syndrome. In adults they are usually sun induced, on back of hand or back. Can get a solitary dark one

- on the lower lip after sunburn. Differential of dark ones: melanoma. May require excision to differentiate
- Idiopathic Guttate hypomelanosis: pale spots in the shape and distribution of largish freckles on sun damaged skin
- Freckle: brown macule. Due to ↑ pigment production but anatomically normal. Fades if sun exposure ceases. Commoner in redheads

Skin Neoplasia

Naevi and Melanoma

- Naevi = hamartoma of the skin. With respect to melanocytes, a benign neoplasm

Melanocytic Naevi

- Normal skin: epidermal cells, plus melanocytes, Langerhans cells (Antigen Presenting Cells –APC), prickle cells and merkel cells (sensory receptors)
- Benign melanocytic naevi:
 - Junctional: epidermis only, early active growth to <0.5 cm. Can be non-pigmented. Overgrowth of melanocytes in nests along the junction of the dermis and epidermis.
 - Compound: epidermis and dermis, older active growth (moles on palms, soles and genitalia stay junctional)
 - Intradermal: stopped growing, loss of tyrosinase → small and pale. Don't have contact with the epidermal junction (ie are deep). Don't become malignant – must have junctional activity to do this
- Dysplastic melanocytic naevi (Atypical Mole Syndrome):
 - Uncontrolled proliferation without malignancy (> 100 with at least one Dysplastic more or a mole > 0.5 cm)
 - Mostly benign with possibility of malignancy
 - If have > 100 moles, 100 to 200 times normal risk
 - Risk of melanoma proportional to the number of moles, plus family history and degree of atypia
 - Management:
 - Self checking each month
 - Annual doctor check (to make sure they're self checking)
 - Most moles that change aren't melanoma, but if suspicious need to remove it
- Halo naevi: Fairly common, especially in kids. Depigmented symmetrical halo around the mole, but the mole is normal (cf depigmented melanoma where pigmented lesion is not normal and not central)
- Pathogenesis: ?Somatic mutation
- Differential:
 - Melanoma
 - Dermatofibroma: feels firm
 - Seborrheic keratosis: altered texture

Melanoma

- Host Risk Factors: Skin colour, Naevi, Atypical naevi, DNA repair, Immune status
- Environment Risk Factors: UV light (geography, season, time), behaviour. Risk from sun determined by age 15. After that sunscreen mainly protects against squamous and basal cell carcinomas
- Epidemiology:
 - 1 – 3% of childhood cancers
 - Females 14/100,000, males 9/100,000. Difference is in the distribution on the legs
- Spotting them:
 - A: asymmetry
 - B: border irregular – e.g. growing a peninsular
 - C: colour – 3 or more, colour not symmetrical, areas of black, variegated
 - D: dimension > 0.6 cm (although you can get smaller melanomas, and most larger lesions aren't melanomas)
 - E: elevated → ↑dermal penetration (but most are initially flat – superficial spreading melanomas)
 - Usually asymptomatic: don't bleed until late (ie take bleeding seriously) and don't usually itch
- Watch out for:
 - Changes: but moles can change for lots of reasons. And patients aren't good at detecting changes (either miss them or think they've changed when they haven't)

- Bleeding, itching and halo (although can get two tone moles – OK if symmetrical)
- Progression:
 - Radial Growth Phase: initially growth is along the dermo-epidermal junction and within the epidermis
 - Vertical Growth Phase: Growth into the dermis → malignant cells in contact with lymphatics and capillaries → metastasis
 - Nodular melanoma: bad news
 - Acral Lentiginous Melanoma: on palms and soles
- Differential:
 - Benign mole
 - BCC
 - Seborrheic keratosis: stuck on appearance, monotone and symmetrical, greasy surface, numerous
 - Angiokeratomas
 - Dermatofibroma: firm, round, monotone
 - Any lesion under a nail (usually thumb) is a melanoma or SCC until proven otherwise
- Pathology:
 - Features of malignant cells: irregular, hyperchromatic, large N:C ratio, mitoses (blackberry nuclei), abnormal number of mitosis
 - Radical/Superficial/Horizontal growth phase: cells in contact with dermis, don't metastasise
 - Vertical growth: mass of atypical melanocytes infiltrating dermis, lymphocytes, not necessarily pigmented, metastasises
 - Will always have junctional activity. If they only exist deeper in the dermis then they're not malignant.
- Prognosis:
 - Breslow tumour thickness (> 0.76 cm bad) or Clarke's levels (grade 1-5, 3 ~ Breslow 0.76, bigger = worse)
 - Ulceration > 3 mm (bad)
 - High mitotic rate (bad)
 - Regression an indication of metastasis (bad)
 - Tumour infiltrating lymphocytes (bad)
- Treatment: surgical excision
- Hutchison's Freckle: freckly 'in-situ' melanoma. Usually on face, tan macule that slowly enlarges and develops a geographic shape, multicoloured in time. Malignant change of melanocytes along the epidermis border but no infiltration. Takes years to become invasive. On sun damaged skin. On elderly watch for a while. Now showing up on younger people – excise before they get too big

Other Naevi

- Epidermal Naevi:
 - Defined according to their predominant cell type
 - Circumscribed distribution over a part of the body surface, usually dermatomal
 - Any size, never cross the midline, uncommon on face and head
- Sebaceous Naevi: hamartomas of predominantly sebaceous glands. Usually on scalp (lesion is bald). Raised, velvety surface, present at birth, usually small. ↑Risk of basal-cell carcinoma, but no longer prophylactically excised
- Dermal Melanocytic naevus (Mongolian spot): macular blue-grey pigmentation present at birth, over sacral area in Mongoloid and some other races. Looks like a large bruise. Rarely persist into adulthood.
- Congenital naevocellular naevus: Small is < 1.5 cm, intermediate = $1.5 - 20$ cm, large is > 20 cm. If over lower sacrum → ?spinabifida occulta. May arise or darken in puberty. Large ones have ↑risk of melanoma
- Spitz naevus: appears in early childhood as a firm, round red or reddish brown nodule. May bleed and crust. Benign. Local excision.

Other Tumours

Benign

- Epidermal cyst:
 - Collection of epidermal cells within the dermis. Either around the base of a hair follicle or from trauma (eg on a builder's hands)

- If it becomes infective → ulcerates and smells
- May be tethered to the epidermis with a central keratin filled punctum
- Treatment: surgical excision for cosmetic or nuisance reasons
- Seborrhoeic Keratosis (= Basal cell papilloma)
 - ↑ Incidence with age, sun exposure, familial tendency, often associated with skin tags
 - Raised, sharply demarcated papule or plaque, shiny, bleeds easily if scrapped. Variable size, ‘stuck on’ appearance with cobblestone or leathery appearance, skin coloured, yellowish or greyish brown/black
 - Results from proliferation of squamous basaloid cells which sit on top of and do not invade the dermis (grow up, compared to BCC which grows down)
 - Histology: hyperkeratosis, well circumscribed, cystic structures within the epidermis filled with keratin
 - Treatment: liquid nitrogen for cosmetic reasons. Fairly harmless
 - Differential:
 - Melanoma – but different surface texture
 - Pigmented solar keratosis: treatment similar so differential not so important
- Keratoacanthoma:
 - Uncommon
 - On lip, up to 1 cm. Other areas up to 2 cm. Develops quickly (eg 4 weeks – too fast to be an SCC) then heals with a scar
 - A ‘self healing squamous cell carcinoma’. Inflammatory reaction at the base – body is rejecting it
- Dermatofibroma (= sclerosing haemangioma):
 - Slightly elevated and pink or brown. Firm, button-like dermal lesion. Usually female
 - Histology: expands into dermis
 - Not malignant – but recurs if not all cut out

Premalignant Lesions

- Actinic keratosis (= Solar Keratosis)
 - Common: 50% of NZers over 65
 - In situ proliferation of dysplastic squamous epidermal cells caused by UV light. Often on face, white
 - Adherent scale, difficult to pick off. Not well circumscribed. Erythematous base
 - May spread within the epidermis, stop growing, recede or progress to invasive squamous cell carcinoma (only 1%)
 - Histology: large, irregular nuclei, overgrowth of epidermis, hyperkeratosis and parakeratosis
 - Indicates sun damage has occurred → person at ↑ risk of SCC, BCC and melanoma
 - No evidence that removal reduces the incidence of cancer – don’t need to treat but often do for cosmetic reasons
 - Differential:
 - Bowen’s Disease: usually larger with a sharper margin
 - Discoid Lupus: erythema or pigmentation more marked, may have a pitted surface, more common in Polynesians
 - Treatment:
 - Reduce sun exposure
 - Examine skin regularly for cancer
 - Remove lesions which are atypical, growing, annoying, unsightly
 - Liquid nitrogen if few in number
 - Efudix (5FU) cream: good for treating a large area – goes red and sore, stop cream then resolution. If you use the cream too long → ulcers, etc
 - Also retinoic acid, laser resurfacing, imiquimod (expensive)
- Bowen’s Disease:
 - More uncommon – but at least as common as SCC
 - 75% are on the leg
 - Erythematous, well circumscribed, 1cm or more
 - Slightly raised plaque with irregular hyperkeratosis. Compared with BCC it’s not so shiny and has no pearly rim. May be bright red
 - May remain stable for a long time. If growing or bleeding or young patient → treat. SCC arises in 3%
 - Differential:

- Solar keratosis
- BCC: shiny surface, pearly border, few dots of pigment
- Psoriasis: silvery scale
- Eczema
- Treatment:
 - Excision
 - Liquid nitrogen – need more aggressive freeze than SK, on leg may ulcerate
 - Leave and watch

Malignant

- Basal cell carcinoma:
 - Most common malignant tumour
 - Nodular BCC:
 - Flat and paler than surrounding skin, pearly or translucent, shiny. May have telangiectases over the surface
 - Progresses to 'rodent ulcer' (ulcer with raised, rolled edges)
 - Often on bridge of nose where glasses sit
 - Differential:
 - Intradermal naevus: Don't have the shiny, stretched look of a BCC
 - SCC: usually in badly damaged skin, and not translucent
 - Superficial BCC:
 - Red plaque +/- atrophy +/- dots of pigment. Usually well circumscribed. Raised rim. Less shiny. Commonest on back, arms, legs, behind ears
 - Most common form of BCC
 - Differential:
 - Eczema: weepy, fissured surface, itchy (BCC isn't), atypical sites for a BCC
 - Psoriasis: silvery scale
 - Bowen's disease: duller surface with more hyperkeratosis
 - Don't metastasis but does invade. Won't kill you (at least quickly)
 - Histology: basophilic (blue) cells, palisaded around the edge
- Squamous cell carcinoma:
 - Skin coloured or purplish nodule/plaque which may ulcerated
 - On badly sun damaged skin – dorsum of the hand, bald scalp, lower lip (BCC's uncommon on these sites)
 - Surface may be hyperkeratotic or warty. Margins less well defined than BCC
 - May have cutaneous horn. Fleshy layer at the base of the horn differentiates it from benign lesions
 - Commonly misdiagnosed as BCC
 - If neglected will invade (claw-like infiltration)
 - 4% metastasise
 - On sun exposed areas, may have cutaneous horns
 - Histology: hyperkeratosis

Ulcers

Venous Stasis Ulcers

- 70 – 90% of ulcers on lower extremities are due to venous insufficiency (eg varicose veins)
- Below the knee, never on the sole of the foot, usually around the malleoli
- Unlike ulcers due to arterial insufficiency, will have good peripheral pulses and no peripheral neuropathy
- Usual isolates: *S aureus* and/or various G –ive bacilli (including *Pseudomonas aeruginosa* and other aerobic G-ive's)
- Treatment: in absence of extensive surrounding cellulitis or systemic signs, there is no role for systemic antibiotics

Pressure Ulcers

- = Skin necrosis and ulceration as a result of pressure induced ischaemia
- Incidence over a 3 week period of bed and chair bound patients is about 8 %
- Critical factors in their development:

- Pressure: Muscle and subcutaneous tissue are more vulnerable than epidermis. Pressure leads to venous, arteriolar and lymphatic occlusion. Especially over bony prominences
- Shearing: Sliding of adjacent surfaces (eg sacral skin on underlying bone) → ↑ vulnerability to pressure induced obstruction
- Frictional forces: Eg from being pulled across sheets → intra-epidermal blisters
- Moisture: eg urinary incontinence, also sweat and faeces. ↑Risk of pressure sores 5 times
- Risk factors: age (loss of blood vessels, epidermal atrophy etc) and immobility
- Staging:
 - 1: irregular, ill-defined area of soft tissue swelling, induration and heat. Reversible
 - 2: Plus inflammatory and fibroblastic response. Extends through dermis and into subcutaneous fat. Reversible
 - 3: Plus undermining of edges
 - 4: Plus underlying muscle and bone
- Infection. All pressure areas become contaminated. Impairs healing. Can lead to bacteraemia (usually polymicrobial) with high mortality
- Site: most at the sacrum, heel, ischial tuberosities and greater trochanter
- Management:
 - Prevention (responsibility of all involved professionals)
 - Decreasing pressure: change of positioning, padding, alternating air cell mattresses
 - ↓Friction: appropriate bed clothes, no particles in bed (eg food)
 - ↓Moisture: Pads, catheters, reduced sweating
 - ↓Shearing: avoid shearing positions (eg propped up in bed)
 - Established sores: Good nutrition, oral vitamin C, ?topical antibiotics (but ↑resistance), saline dressings + variety of preparations/dressings. If stage 3 or 4 then consider debridement or skin grafts

Other Ulcers

- Ischaemic ulcers:
 - Large artery disease: usually lateral side of the leg, pulses absent
 - Small vessel disease (eg vasculitis): palpable purpura
- Malignant ulcer: eg basal cell carcinoma (pearly translucent edge), squamous cell carcinoma (hard everted edge), etc
- Neuropathic ulcer: painless penetrating ulcer on the sole of the foot due to peripheral neuropathy (eg diabetes, leprosy)
- Underlying systemic disease: Diabetes, pyoderma gangrenosum, rheumatoid arthritis, lymphoma

Inflammatory skin lesions

Psoriasis

- Epidemiology:
 - Begins at any age
 - ~2% of the population
- Chronic characterised by rich red, erythematous silvery scaly plaques. May or may not itch
- May be inherited (autosomal dominant with mixed penetrance)
- Precipitated or aggravated by:
 - Cigarette smoking and alcohol consumption
 - Strep infection
 - Trauma (Koebner phenomenon)
 - Hypocalcaemia
 - Drugs: lithium, beta blockers, Antimalarials, withdrawal of systemic steroids
 - Stress
- Characterised by rapid turnover of epidermis. Normally 28 days, reduced to 4 days → parakeratosis
- Histology: epidermal squamous cell hyperplasia, neutrophil accumulation
- Psoriasis vulgaris:
 - Elbows, knees, scalp
 - Histology: parakeratosis, acanthosis, focal thinning, oedema of dermal papillae, micro-abscesses in the stratum corneum
- Pustular psoriasis:

- Abscess formation within the epidermal layer → widespread sloughing → risk of infection/electrolyte imbalance
- Generalised (rare and life-threatening) or localised (most commonly palms and soles)
- Nail involvement: pitting, discolouration, subungual hyperkeratosis and onycholysis (especially lateral)
- Differential:
 - Bowen's disease: usually over leg
 - Superficial BCC
 - Eczema: may show Lichenification or fissures or vesicles
 - Lichen planus
 - Fungal: do a scraping
 - Discoid Lupus: face, leaves scars, has plugs of follicular hyperkeratosis
 - Seborrheic dermatitis
- Treatment:
 - Mild steroid creams for face and flexures
 - Stronger steroid creams for short periods on trunk and limbs (but rebound flare up)
 - Coal tar creams: messy and smells
 - Dithranol + salicylic acid in white soft paraffin
 - Scalp: steroid of Betnovate strength to shift scale then a maintenance cream
 - UVB treatment
 - PUVA: Psoralen tablets 2 hours prior to UVA treatment twice a week. Effective but may have to travel
 - If severe: methotrexate, Acitretin, cyclosporin, etc

Bullous Lesions

- Epidermis sloughs off dermis
- Intraepidermal: if any of the epidermis is left attached
 - Burns
 - Herpes
 - *Pemphigus*:
 - 40 – 60 years, very fragile blisters skin, and also on *oral* and nasal mucosa
 - Less common than Pemphigoid but more serious (40% mortality)
 - Histology: BM is intact, acantholysis
 - Pathogenesis: Autoimmune reaction to desmosomes in the epidermis → infection etc. IgG **above** the basement membrane. Chicken-wire pattern on immunofluorescence within the epidermis
 - Types:
 - Pemphigus vulgaris: suprabasal lesions. More serious of the two. Mucosal and scalp involvement, more fragile blisters, looks like burn. Generalised bullous phase ~ 5 months after the onset of oral lesions. Heals without scarring. Patients are ill
 - Pemphigus foliaceous: acanthosis only in the superficial epidermis. Small flaccid blisters, rupture leaving erythematous lesion, heals with crusting and scarring. Face, scalp, chest and back. Oral lesions not common
 - Treatment: High dose steroids
- Subepidermal:
 - *Pemphigoid*:
 - Smaller, localised, sturdy, grape-like blisters, generally rest of skin remains in tact. Ruptured lesions heal rapidly. *No oral involvement*
 - May have only urticarial lesions with no blisters, or just vesicles, or eczema like appearance
 - Usually self-limiting, chronic relapsing, > 60 years. Can become generalised
 - Histology: Epidermis lifts in total at the dermo-epidermal junction
 - Pathogenesis: IgG **in** the BM, linear stain with immunofluorescence
 - Differential:
 - Diagnosis of bullae difficult. Usually need to refer, and histology (*prior* to treatment) usually necessary
 - Pemphigus (flaccid bullae with mucosal involvement)
 - Eczema (but not itchy)
 - Russian hog weed et al

- Treatment:
 - Systemic steroids: may need 20 – 40 mg per day. Unsuitable for long term use → problem especially in the elderly
 - Topical steroids if localised
 - Tetracycline 1 – 2 g per day, especially in elderly
 - Other immunosuppressive treatment (eg methotrexate)

Discoid Lupus Erythematosus (DLE)

- = Mild end of Lupus spectrum and much more common than SLE. Mild skin rash, normal serum ANAs and ENAs
- Rash usually on the face, usually crosses the nose, sometimes scalp, ears, nose, arms
- Erythematous plaques varying from several mm to several cm. Adherent scale (not flaky like eczema) and pitted surface. Rough feel, doesn't itch. May heal with hyperpigmentation or white scar. Scarring alopecia
- Alopecia in scalp lesions which is normally permanent
- More common in Polynesians and Maori, F > M
- Characteristic histology and direct immunofluorescence (DIF) +ive
- Differential:
 - Eczema (doesn't scar, uncommon to get discoid eczema on face, eczema can be weepy)
 - Solar keratosis or Bowen's (but patient usually too young for these)
- Treatment:
 - Topical or intralesional steroids: fairly potent ones but be careful on the face. Systemic if widespread
 - Sun protection
 - Antimalarials (eg hydroxychloroquine. SE: eye problems → regular check-ups)
 - Topical Retinoids – also ↑ penetration of topical steroids
- See also Systemic Lupus Erythematosus, page 278

Morphea

- Localised cutaneous scleroderma, occurs any age but especially 20 - 40
- Thickened dermis with dense collagen, progressive loss of subcutaneous fat
- Waxy, ivory coloured skin without hair or sweating
- Vary in size from 2 – 15 cm with lilac coloured edge
- Any site, especially the trunk
- Tend to improve over time (years)
- Treatment: intralesional steroid
- See Progressive Systemic Sclerosis (PSS), page 280

Vitiligo

- Slowly progressive amelanotic macules, initially on sun exposed areas. Usually symmetrical
- Affected areas prone to sunburn
- ?Autoimmune
- Associated with family history and other autoimmune disorders (eg alopecia areata)
- In 50% develops before age 20
- Differential:
 - Tinea versicolor (but hypopigmented, not amelanotic, and scaly)
 - Pityriasis alba (but hypopigmented, not amelanotic, and scaly)
- Treatment: usually unsatisfactory
 - PUVA or narrow band UVB (may need 2 or 3 treatments a week for a year)
 - Various surgical procedures

Acne

- Inflammatory disease occurring in and around the sebaceous glands, generally affecting the face, also the chest and back. Characterised by papules and pustules, or by cyst and other more specific lesions. Deeper lesions are associated with scarring: hypertrophic, keloidal or depressed
- Differential:
 - Rosacea
 - Perioral dermatitis

- Acneiform drug eruptions

Pathogenesis

- Four factors:
 - Increased sebum production by the sebaceous glands (normally produced to maintain epidermal hydration)
 - Cornification (→blockage) of the pilosebaceous duct: abnormal keratinisation and desquamation of follicular epithelium combine with increased amounts of sebum production to obstruct the duct.
 - Bacterial proliferation - abnormal colonisation of the follicle duct by *Propionibacterium acnes*. But severity not proportional to number of bacteria
 - Inflammation
- If the obstruction is closer to the skin surface it will form open comedo and oxidation of the fatty material causes discolouration (blackhead). A closed comedo (white head) occurs when the duct is blocked at a deeper level
- Acne is dependent on:
 - Genetic factors (high concordance in monozygotic twins)
 - Hormonal factors: androgens → sebum production
 - Environmental factors: aggravated by humidity, some cosmetics and oils (block pilosebaceous orifice)
 - Diet rarely implicated
- Usually starts in adolescence and resolves by mid 20s (starts earlier in females and is more persistent)

Management

- *Reassurance*: Treat as a physical and psychological disorder. Undermines patient's self-confidence, especially in the adolescents. Myths of poor diet and hygiene make patients feel responsible and/or guilty - reassured that they are not the cause
- General advice:
 - Avoid humid conditions
 - Avoid occlusive creams and sunscreens
 - Only use moisturisers if the skin is dry
- *Topical agents*. For mild to moderate acne:
 - Comedolysis: most effective option is Tretinoin. Normalises desquamation of the follicular epithelium promoting drainage of pre-existing comedones. This increases penetration of antimicrobial agents
 - Antibiotics such as benzoyl peroxide and erythromycin gel reduce bacterial numbers and inflammation
- Oral agents. Are generally used for severe or persistent acne in addition to topical agents:
 - Antibiotics such as tetracycline, doxycycline, trimethoprim and erythromycin suppress inflammation by inhibiting neutrophil chemotaxis and production of bacterial lipases and proteases. For a minimum of six months with an 80-90% improvement expected after this time. Often recur. SE of Minocycline: vertigo, discolouration of teeth, *grey skin pigmentation*
 - Oestrogens. They have a direct effect on sebaceous gland activity. They are combined with progesterone in an oral contraceptive, which may counteract the effects of the oestrogen
 - Antiandrogens (in a female only) such as cyproterone acetate and spironolactone act peripherally to inhibit androgen stimulation of sebaceous glands and hair follicles. They are useful in mature presenting acne
 - Isotretinoin (Roaccutane)
 - A synthetic Vitamin A derivative that inhibits sebaceous gland activity, reduces *P. acnes* cell numbers, alters follicular keratinisation and is anti-inflammatory
 - At adequate doses permanently cures acne in 80% of cases after 4 – 6 months
 - Highly teratogenic. Women need to be fully informed of the risks, need to have a negative pregnancy test before starting treatment, and need to be on reliable contraception throughout course (i.e. belt and braces) and one month after
 - Causes liver damage and hyperlipidaemia: baseline bloods and then after one month
 - Causes dry lips and maybe nasal mucosa (→ epistaxis), skin and eyes, angular cheilitis
 - < 10% will get aching muscles, depression, hair loss, headaches
 - See Retinoids, page 336

Rosacea

- Cardinal signs in order of importance:
 - Erythema
 - Telangiectasia
 - Papules
 - Swelling
 - Tiny pustules
- On cheeks, chin, forehead, nose and neck, sun exposed sites. Flushing may precede other signs
- Many theories
- May be associated with rhinophyma (bulbous swelling of the nose)
- Minor ocular involvement in 50%: especially conjunctivitis, may blepharitis, etc
- Treatment:
 - Systemic or topical antibiotics (as per acne)
 - Retinoids
 - Metronidazole

Perioral Dermatitis

- Mainly young women
- Cause a mystery. ?Steroids implicated
- Starts in nasolabial fold and spreads to involve the perioral area. Minute papules and pustules on an erythematous base with some scaling
- Treatment: Systemic tetracyclines or erythromycin until rash gone then for another couple of weeks

Other Skin Lesions

Erythema Multiforme

- Confusion/overlap between Erythema Multiforme (EM), Stephens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) [Later two at the severe end of the spectrum]
- Varying degrees of mucosal involvement and rash
- Typical lesion: target lesion – dull red macule or maculopapule 1 – 2 cm across, erythematous rim with cyanotic or purpuric centre. May be blistering. Typically affects acral areas (dorsal hands, feet, palms, soles, forearms, legs). Usually crop over a couple of days and fade after a couple of weeks.
- Trunk only in extensive reactions. Also if severe: erosions, haemorrhagic crusting, lesions uncomfortable (not usually painful). May affect cornea. May get systemic upset (fever, anaemia, etc)
- Histology: vacuolar degeneration of lower epidermis
- Provoking factors:
 - HSV – major cause. Rash worst at periphery (+/- oral mucosa). Will get it with subsequent outbreaks as well. History: Do you get cold sores?
 - Mycoplasma (<1% of EM)
 - Drug reactions – more likely if severe outbreak. Not typical targets (eg red blotches), on trunk as well as acral, may be blistered. Implicated drugs: anticonvulsants, sulphonamides, NSAIDs, allopurinol. Stops drugs if at all possible. Treat like a burn. Steroids controversial
 - Idiopathic

Erythema Nodosum

- Lesions: 2 – 4 cm, erythematous, tender, especially on shins but also on thighs or forearms. A little raised. Look like purplish bruises
- Number from 2 – 50 (usually 5 – 6), erupt over 10 days and subside over 3 – 6 weeks
- Regress with bruise like yellow/green colour changes
- Systemic signs: fever, generalised aching and malaise
- Due to deposition of immune complexes in and around venules in the deep dermis
- Causes:
 - Kids: Streptococcal infection
 - Sarcoidosis (rare in kids)
 - TB
 - Cat scratch disease
 - Yersinia
 - Some drugs

- Differential:
 - Nodular vasculitis (tend to ulcerated, don't heal with bruise like changes)
 - Meningococcal or gonococcal septicaemia (smaller lesions, often purpura, ill patient)

Erythema Toxicum Neonatorum

- Up to 50% of full term infants (less if preterm), occur up to 4th day
- Erythematous macules, wheals, papules and pustules – few to several hundred
- Face, buttocks, torso, proximal limbs, not palms or soles
- Usually resolve in several days
- Cause unknown
- Differential: HSV

Urticaria

- = Hives or welts. Intensely itchy.
- Relationship to allergy and atopy:
 - More likely in atopy
 - 50% related to allergy – type 1 only ⇒ exposure 15 – 30 minutes prior to onset and last < 24 hours ⇒ careful history
 - Allergy likely to be all over, and no further outbreak for weeks/months
 - Most chronic urticaria is non allergic
 - Some foods/drugs may cause urticaria without immune involvement (ie histamine release without IgE involvement)
- Common causes:
 - Idiopathic – common
 - IgE mediated:
 - Food: peanuts, strawberries, milk, eggs
 - Animal dander: horses, cats
 - Physical: pressure, cold, heat
 - Complement mediated: hereditary angioedema and blood transfusion reactions
 - Mast cell releasing agents: opiates, penicillins
 - Prostacyclin inhibitors: Aspirin, NSAIDs
 - Infections: cause of 80% of acute childhood urticaria (eg hepatitis)
 - Serum sickness: type 3 reaction. Drugs, especially penicillin. Fever, raised ESR, starts within 5 – 20 days of exposure and lasts 5 – 28 days. See Allergy, page 309

Papular Urticaria

- Hypersensitivity to an insect
- Itchy, urticarial weal → firm itchy papule
- Usually gone in a day to two, may persist for months
- Grouped in clusters, and develop crops at irregular intervals
- Treatment: try insect repellent
- If dark skin, may be post-inflammatory hypopigmentation

Alopecia Areata

- Circumscribed areas of hair loss but skin normal.
- Presentations:
 - Often scalp – with a few bald areas 1 – 3 cm
 - Loss of all scalp hair is alopecia totalis
 - Loss of hair at all sites is alopecia universalis
- Not a diagnosis
- Autosomal, autoimmune dominant disorder with variable penetrance
- Duration < 1 year in 50 %, relapse common. Kids get it worse
- Associated with Atopy, Downs, Hashimoto's Disease, Pernicious Anaemia, Addison's Disease, Vitiligo
- Treatments include local steroids, topical minoxidil (antihypertensive), etc
- Differential diagnosis: all produce circumscribed hair loss, but skin itself is abnormal
 - Fungal infections
 - Anything causing scarring (eg skin cancer)

Keratosis Pilaris

- Common. More common in atopics
- Small whitish plugs of keratin obstruct the follicle mouth. Usually extensor surfaces. Feels like sandpaper
- Variable perifollicular erythema
- Facial involvement usually resolves in teens. Elsewhere can persist until middle age
- Autosomal dominant with variable penetrance
- Differential: Acne (shouldn't feel like sandpaper)
- Treatment: mild steroids, urea creams, salicylic acid creams, etc

Granuloma Annulare

- Ring of smooth, firm, skin coloured or slightly purplish papules from 1 – 5 cm. No scaling (cf ring worm which is) or blistering (\Rightarrow epidermis fine)
- Enlarge centrifugally, with beaded rim gradually flattening until it disappears without trace within 2 years
- Dorsal surfaces of feet, hands and fingers are the commonest sites
- Lymphohistiocytic granulomata
- Mainly children and young adults
- Can treat with intra-lesional steroids

Lichen Planus

- Occurs in 30 – 60 year olds. Insidious onset, can be explosive, localised or generalised. In 80% resolves in 18 months
- Clinically: flat topped papules, discrete or coalescing. White lines on papules = Wickham's Striae. Can also get annular, hypertrophic, atrophic or even bullous forms. Should linear lesions characteristic. Itch variable. Rash resolves with hyperpigmentation. Can be painful on lips or genitals.
- Looks like everything else. Differential:
 - Plane warts
 - Eczema
 - Drug reaction: gold, quinine, thiazides, etc
 - Treatment: Acitretin, steroids, miscellaneous

Tuberous Sclerosis

- Disorder of haematoma formation: especially in eye, brain, skin, kidney and heart
- Skin lesion:
 - Angiofibromas: appear from 3 – 10, firm, discrete red/brown telangiectatic papules, 1 – 10 mm, cheeks and chin
 - Periungual fibromas: smooth skin coloured excrescences emerging from the nail folds
 - Shagreen patch: skin coloured plaque in lumbosacral region
 - Oval white macules (Ash-leaf-macules) seen under Woods light. But also similar lesions common in normal kids
- Classically (but not invariably) seen with epilepsy and mental retardation ('zits, fits and nit-twits')
- Autosomal dominant with variable penetrance, 50% are new mutations
- Prevalence ?1/10,000

Neurofibromatosis

- Look like intradermal naevi but soft
- Type 1: commonest, 1/3000, Autosomal dominant, 30% new mutations
- Type 2: 2 or more of:
 - 6 or more café-au-lait macules over 5 mm in pre-pubertal patients
 - 2 or more neurofibromas
 - Freckling in axillary or inguinal regions
 - Optic glioma
 - Others
- May lead to short stature, macrocephaly, kyphoscoliosis, intellectual handicap, endocrine problems (precocious puberty, acromegaly, Addison's), neuro tumours (optic nerve glioma, astrocytomas), etc
- NF2: characterised by bilateral acoustic neuromas
- See Other Congenital Skeletal abnormalities, page 620

Ichthyoses

- All genetic
- Ichthyosis vulgaris: common, usually mild. Entire skin is scaly. Controlled with moisturisers
- Rare sorts: Collodion Baby, Bullous and non-bullous ichthyosiform erythroderma, lamellar ichthyosis, X-linked ichthyosis, Harlequin fetus

Erythroderma

- Inflammatory skin disease involving 90% or more of the body surface. Don't call it Exfoliative Dermatitis – meaning is unclear
- May have sudden onset over weeks or days. Scaling varies in degrees. Itch varies
- Well unwell, feel hot or cold even though temperature normal. Hypoalbuminaemia and oedema common
- Fatal in 20 – 40% due to pneumonia, septicaemia, cardiac failure
- Cause:
 - Eczema: 40%
 - Psoriasis: 25%
 - Lymphoma, leukaemia: 15%
 - Drug reaction: 10%
 - Unknown: 10% (usually elderly)
- History usually helpful, histology usually unhelpful
- Management: monitor fluid balance, rest, nutrition (shedding lots of protein), Moisturiser, careful use of steroids, methotrexate, etc.

Epidermolysis Bullosa

- All rare
- Variety of inherited forms. An acquired form exists
- Can be localised or generalised
- Types:
 - Generalised simple autosomal dominant epidermolysis bullosa
 - Junctional EB
 - Autosomal Recessive Dystrophic EB
 - Autosomal dominant dystrophic EB

Incontinentia Pigmenti

- X-linked dominant, usually lethal in males
- Presents within first 2 months
- Tense bullae on limbs then red nodules or plaques on limbs and trunk
- Pigmentation ranges in colour from blue-grey to brown

Pharmacology

- Topical treatment → ↓systemic side effects
- Penetration of drugs into the skin depends on:
 - Barrier function (↓ with age and disease)
 - Nature of the vehicle (greasy better)
 - Interaction of the drug and vehicle
 - Hydration
 - Patient compliance (especially if sticky, smelly or staining)
- Types of vehicles:
 - Liquids: solutions, emulsions (oil in water or water in oil), emulsion, suspension
 - Semi-solids: ointments (no water), gels, creams, pastes
 - Greases: oils, waxes, mineral greases (eg vasoline), macrogols

Treatments

- Coal tar: in psoriasis, sometimes eczema. Therapeutic agent unknown

Topical Steroids

- Double the concentration doesn't necessarily double the efficacy
- Potency related to receptor binding. Modulates messenger RNA production

- Anti-inflammatory effects involve a wide range of mediators
- Side effects:
 - Epidermal thinning
 - Melanocytic inhibition
 - Reduction in collagen synthesis and ground substance → striae and intradermal haemorrhage
 - Vascular effects: initial vasoconstriction → rebound vaso-dilation → oedema, inflammation
 - Inhibition of pituitary-adrenal axis if excessive use or potent
- Grouped into 4 classes according to “potency” – based on vasoconstrictor assays not efficiency

Antifungals

- Griseofulvin
 - Only one till recently
 - Poorly absorbed orally, carried to skin through sweat
 - Fungistatic
 - Rapidly cleared from the skin → have to continue till condition cleared
 - Headaches and nausea common
 - Only effective against dermatophytes, not yeasts (eg candida)
 - Lamisil and itraconazole: effective against fungi + yeasts
- Itraconazole (=Triazole)
 - Fungistatic
 - Absorption dose dependent, take with a fatty meal
 - Persists in skin for 4 weeks and in nails for up to 6 months after 3 month course
 - P450 interaction
 - GI side effects in 7 %
- Terbinafine (=allylamine)
 - Fungicidal
 - Well absorbed orally
 - Adverse effects in 10%, no P450 effect
- Use:
 - Cochrane review: no evidence that topical antifungals are of value in fungal toenail infections
 - Skin infections of the feet: allylamines better than azoles, but much more expensive

Retinoids

- Retinol (vitamin A): metabolised by the liver to retinal, then oxidised to retinoic acids. β carotene can also be converted into retinol
- A hormone: binds to nuclear receptors
- Modifies the expression of a variety of genes involved in cell growth and differentiation
- Induces epidermal hyperplasia and desquamation (efficacy without peeling unlikely)
- Thins the stratum corneum, ↑ dermal capillaries, etc etc, promotes hair growth
- Isotretinoin (=Roaccutane, Oratane, 13 cis retinoic acid)
 - Lipophilic (\Rightarrow take with food)
 - Teratogenic: contraception till 1 month afterwards
 - Side effects: dry skin, mucosa, photo-sensitive, aching muscles, headaches
- Acitretin (=neotigason)
 - Inhibits formation of retinoic acid from retinol.
 - Used in Psoriasis
 - Teratogenic for 2 – 3 years afterwards, also reduces efficacy of oral contraceptives
 - Plus dry skin, mucosa, photo-sensitive, aching muscles, headaches

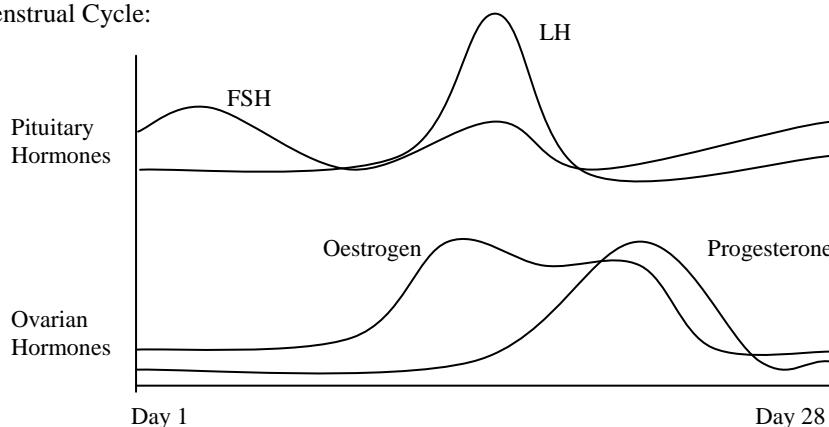
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Gynaecology

Physiology

- GnRH:
 - 10 amino acids – only lasts seconds \Rightarrow requires portal circulation
 - Pulsatile release
 - Stimulates release of FSH + LH
 - Inhibited by progesterone (strongest inhibitor), PRL, inhibin, testosterone, oestrogen, stress
- FSH: acts on germ cells
- LH: acts on supporting tissue:
 - Male: Leydig cells \rightarrow testosterone
 - Female: Thecal cells \rightarrow testosterone \rightarrow acted on by aromatase (produced by granulosa cells) \rightarrow oestradiol
- Oestrogen: three types:
 - Oestradiol: ovary
 - Produced by follicles
 - $\rightarrow \uparrow$ Mucus
 - -ive feedback on FSH
 - Above a threshold $\rightarrow \uparrow$ LH
 - Unopposed oestradiol causes endometrial hyperplasia – growth without the maturing effect of progesterone
 - Oestriol: placenta
 - Oestrone: metabolised from androgens (eg testosterone) by adipose tissue
- Female fetus has several million eggs, by puberty has 300 – 400 eggs
- Follicle at ovulation is 2 cm
- Infection control:
 - Sperm carry bacteria and viruses into uterus. If mucus inhibits sperm $\rightarrow \downarrow$ infection, which would otherwise cause inflammation and \downarrow chances of implantation
 - \uparrow Oestrogen \rightarrow Vaginal epithelium thickens during cycle $\rightarrow \uparrow$ glycogen $\rightarrow \uparrow$ lactobacilli $\rightarrow \uparrow$ acidity $\rightarrow \downarrow$ other bacteria
- Menstrual Cycle:



- Inhibin from developing follicle suppresses FSH compared with LH \rightarrow LH surge
- Phases for uterus endothelium: menstrual \rightarrow proliferative/follicular \rightarrow secretory/ progestational
- Human Chorionic Gonadotrophin (hCG) from implanted zygote signals corpus luteum to continue progesterone production.

History

- Introduction Data:
 - Age
 - Gravidity = total number of pregnancies
 - Parity = # of deliveries (multiple births = 1 delivery – but definitions vary...). E.g. P1(SB) = one stillbirth. P1(twins). Eg: G4P2 (+TOP + SAB). SAB = Spontaneous Abortion.
 - LMP

- +/- Martial status
- Presenting complaint: recorded as direct quote from the patient. Give them time to tell you. Stop and listen!
- History of presenting complaint. Include:
 - Bleeding:
 - Quantity (eg # of pads per day – but ask why they change – 1 per hour too much), double protection needed (eg tampon and pad), soaking through, etc
 - Duration
 - Quality. Bright red ⇒ fast flow. Brown ⇒ slow flow. Clots
 - Timing: with menses, inter-menstrual, post-coital
 - Always consider anaemia, look for signs, do FBC if indicated
 - Pain:
 - Location (be specific)
 - Radiation
 - Circumstances (related to menses, meals, activity, time of day). Want to differentiate from bowel and bladder pain
 - Character: sharp, dull, continuous, intermittent, severity
 - Relieving factors: position, medication
 - Vaginal Discharge:
 - Duration
 - Relationship to menses
 - Colour, odour, consistency
 - Associated symptoms: itch, burn, dyspareunia, vulvar irritation
 - Response to treatment, if any
 - Urinary symptoms:
 - Incontinence: stress or urge
 - Frequency, urgency
 - Dysuria
 - Haematuria
- Past Gynaecological History:
 - Age of menarche – probably not a big deal – were you significantly younger or older than friends
 - Menses: Frequency (normal 21 – 35 days) and duration (normal 3 – 7 days), regularity (some variation normal). NB:
 - First day of bleeding = 1st day of menstrual cycle. Teenagers will often give their period length as first day without bleeding to first day of bleeding – check understanding
 - Ovulation is 12 – 16 days before the start of the next period (determined by timing of the following period, not the prior period). Fertile for 5 – 7 days before ovulation
 - If post-menopausal, when did periods stop and are there any symptoms
 - Past gynaecological problems or procedures
 - ? Sexual history, currently sexually active
 - Current/past contraception
 - Past STD's, UTIs,
 - Incontinence
 - Smear history: last smear date, any abnormal
- Past Obstetric History (mainly for obstetric history): See History and Antenatal Booking, page 355
- Past Medical and Surgical History (and maybe very brief systems review)
- Medications:
 - Remember vitamins and non-prescription meds – may be bad in pregnancy
 - Allergies
- Family History: Sister or mother with fertility, pregnancy or gynaecological problems
- Social History:
 - Marital/relationship status
 - Sexual activity, sexual orientation ('Are you in a relationship with a man or a woman'), number of partners. To avoid embarrassment, just ask straight
 - Cigarette, alcohol and recreational drug use
 - Occupation
 - ?Victim of interpersonal violence (but don't introduce it in a crisis situation). See Suspicion of Abuse or Interpersonal Violence, page 343

- Gynaecological write-up: [name] is a [age] year old G_P_ LMP (date) who presents complaining of (PC). Then HPC, including all pertinent (+) and (-) and any relevant past medical, surgical or gynaecological information.

Exam

- Explanation while dressed. Check experiences with past exams
- Ensure chaperon if male
- Have available: light, additional light source and mirror for the patient
- Check bladder is empty
- Clear instructions to patient on what clothes to remove and position. Cover with sheet
- Position: flat on back on firm surface, unless prolapsed, obese or on a soft bed, in which case left lateral position (like recovery position) with right knee drawn up
- Pulse: indicator of anxiety
- BP
- General physical exam as indicated
- Vaginal Exam:
 - Bivalve Speculum: warm and check temperature. Introduce at 45 degrees then rotate. Use narrow speculum for nulliparous, wider speculum for multiparous, and paediatric for child or sometimes post menopausal. Use Sim's Speculum for prolapsed. Warm blade, little (preferably no) lubricant if doing a smear.
 - Check size, shape, position and appearance of cervix, view transformation zone and os. Nulliparous or multiparous cervix
 - Bimanual:
 - Check uterus for size, shape, consistency, tenderness and mobility
 - Check adnexae for abnormal swelling or tenderness
 - Normal tube and ovaries are not palpable
- Explain results when fully dressed

Contraception

- Ideal contraceptive is 100% effective, only desirable side-effects, readily reversible, and able to be used un-supervised
- Reference: OHCS + numerous pamphlets
- For a younger person wanting to start on the pill:
 - Discuss the possibility of coercive sex, especially if under 15
 - Discuss the emotional and physical consequences of sex
 - Ask about prior contraceptive use
 - Ask whether they want to become pregnant – establish a context for motherhood in terms of the next 5 years and their life goals
 - Find out their thoughts about birth control (many myths: birth defects, ↓ fertility)
 - Inform about all methods
- Risk assessment questions:
 - Current sexual history
 - Past problems with weight gain
 - Acne
 - Headaches/migraines
 - Dysmenorrhoea/irregular menses
 - Nausea/abdominal pain
 - Diabetes
 - Smoking
 - Personal or family history of DVT
 - Hypertension or IHD

Natural Family Planning

- No intercourse from 6 days before to 2 days after ovulation – free and no drugs
- Monitor fertility by:
 - Checking cervical mucus – clear and stretchy when fertile
 - Temperature ↑ 0.3 C after ovulation (affected by fevers, drugs, drink)
- Success if regular cycles, dedication and self-control

- Peak effectiveness is 2% - usually 10 - 20 % (pregnancies per woman years)

Barrier Methods

- Low health risk, need high motivation, some STD protection
- Condoms, Caps +/- spermicide, female condom (Femidom)
- Don't use oil-based lubricant or anti-thrush cream with condom
- Spermicide gives extra protection

IUCD

- Eg Novagard
- Very effective (failure rate 1-2 per 1000 woman years)
- Inhibit implantation and may impair sperm migration
- Need replacing every 3 – 5 years
- Best in older, parous women in stable relationships
- Contraindications: Pregnancy, high risk for STD, undiagnosed vaginal bleeding, very heavy periods
- Complications:
 - Can be expelled from a nulliparous or distorted (eg fibroids) uterus
 - Ectopic pregnancy more likely (1 in 2000)
 - Associated with PID following insertion or STD
- If she becomes pregnant then must take the IUCD out (little risk of inducing miscarriage). If it's left in then ↑risk of chorioamnionitis, miscarriage or pre-term labour
- Mirena – carries levonorgestrel (a progesterone) → ↓risk of implantation and lighter periods (Good for menorrhagia). Lasts 3 years. 20% experience reversible amenorrhoea. Expensive. Can use with oestrogen only HRT (no ↑risk of endometrial hyperplasia) and avoid progesterone side effects

Combined Oral Contraceptive

- Initial exam should include:
 - Weight
 - Blood pressure
 - Cervical screen if appropriate
- = Oestrogen (usually ethinylestradiol) + progestogen:
 - Oestrogens:
 - Ethinylestradiol (most common), mestranol (which is converted to estradiol. 50 µg mestranol = 35 µg estradiol)
 - High dose = 50 µg estradiol. Low dose is <= 30 µg oestrogen. Adverse effects are dose related ⇒ give lowest dose that gives good cycle control.
 - Progestins:
 - Estranes: norethindrone, ethynodiol acetate, norethindrone acetate (latter two converted to the former)
 - Gonanes: norgestimate, levonorgestrel, desogestrel (gonanes have a longer half-life)
- About 4 * physiological dose of oestrogen
- Triphasic pill: mimic's body's fluctuation in oestrogen but → ↑break through bleeding
- Action: G type mucus + ↓GnRH (→ no ↑FSH or LH surge). 'Puts the ovary to sleep'
- Take for 3 weeks, then pill free for a week → withdrawal bleed
- Benefits of CoC: 99% effective, reversible, lighter periods, ↓PMS, ↓ovarian and endometrial carcinoma (but slightly ↑risk of breast cancer), ↓endometriosis
- Problems: compliance
- Contraindications:
 - > 35 and smoker (death 8 times more common in smokers – but still as safe as childbirth)
 - Any disorder predisposing to venous or arterial problems, eg ↑ lipids, APC resistance
 - Many cardiovascular problems (except mild hypertension)
 - Liver disease
 - Migraine with aura or for > 72 hours (status migrainosus) or requiring ergotamine. Pill → 4 times risk of ischaemic stroke. Contra-indicated in any woman with migraine if > 1 other risk factor for stroke (lipids, BP, diabetes, etc)
 - Pregnancy
 - Undiagnosed uterine bleeding
 - Gross obesity or immobility (stop before major surgery)

- Special precautions: Family history of DVT, ↑BP or breast cancer; epilepsy, diabetes, illnesses causing diarrhoea (eg Crohn's)
- Side-effects: (usually worse when starting the pill), intra-menstrual bleeding, breast tenderness, nausea, ↑ or ↓ weight, mood changes, headaches
- Risks:
 - MI. Risk ↑ sharply over 40 – 1:2500 for non-smokers, 1:500 for smokers.
 - Older progestin: breakthrough bleeding, acne, headache, ↑weight → lead to search for new progestins (ie 3rd generation progestins like gestodene eg in Mercilon, etc)
 - Nausea: due to oestrogen. Take with meal or with a snack at bedtime
 - ↑Blood pressure (rare – but monitor 6 monthly)
 - DVT Risk (Source: Medsafe flier)
 - 35/100,000 on the pill per year develop a clot, one dies ⇒ two deaths per year in NZ
 - Risk increases 3-4 times over population risk on 2nd generation, 6 – 8 times on 3rd generation. Increased risk of Diane 35 and Estelle 35 of 4 times over 2nd generation.
 - No ↑risk with PoP
- Drugs interfering with the pill: liver enzyme inducers (eg anticonvulsants, rifampicin). Consider higher dose pill
- Monitoring: 6 monthly-BP check. Check weight and breasts etc if > 35. Up to date with smears?
- Starting the pill:
 - On day 1 of cycle, or day of TOP, 3 weeks post-partum or 2 weeks after mobilisation after major surgery. Contraceptive cover immediate
 - Breakthrough bleeding is very common – especially in the first 3 months. Can add 20 µg estradiol every 24 hours, 12 hours after the usual pill, for one week.
- Missed pill: 12 hours late OK, after that the seven day rule (also if diarrhoea) – take 7 active pills before unprotected sex (eg if pill free days coming then skip them and go straight onto the next pack)
- Stopping:
 - 66% menstruate within 6 weeks, 98% by 6 months
 - At menopause: Stop at 50 with > 1 years amenorrhoea. CoC masks menopause, so stop at 50 and use non-hormonal method. Little evidence that it's not safe to continue to menopause

Progesterone Only Pill (PoP)

- = Mini-pill
- → Cervical mucus hostile to sperm (G Type mucus) + prevent ovulation in some + ↓tubal motility. Effectively a barrier method. Woman may still ovulate. Small risk of follicular cyst (one that doesn't pop) → pain with full bladder or rectum
- Worst side effect: erratic bleeding. Some women have amenorrhoea. Less risk of weight gain, acne, depression, breast tenderness, headache
- Less effective than CoC (0.3 – 4% failure) – age and compliance dependent
- OK where CoC contra-indicated and in breast-feeding mums (full breast feeding alone is protective for 3 months). For post-partum contraception see Six Week Check, page 374
- Contraindications: History of ectopic pregnancy, breast cancer, liver disease or enzyme inducing drugs
- Must be taken same time each day (+/- 3 hours).
- Starting on the PoP: Alternative precautions for 7 days
- If pill missed then at risk for 2 days. Safe again after 2 days of restarting the pill
- Depot progestogen:
 - Safe, simple and effective (failure rate 0.4 – 1.2 %). Suppress ovulation, G type mucus, ↓ motility and implantation
 - Eg Depot-provera – deep IM 12 weekly, given during first 5 days of cycle, 5 days post partum if bottle feeding, 6 weeks if breast feeding.
 - Contraindications: pregnancy, abnormal undiagnosed vaginal bleeding, acute liver/cardiac disease
 - Advantages: no oestrogen, ↓PMS, secret, no compliance problems, good with GI disease, Ok with breast feeding, etc... Particularly good around major surgery, epileptics, after vasectomy and bowel disease
 - Problems: irregular bleeding – usually become amenorrhoea, also weight gain and acne. May also ↑depression and ↓libido. Median delays of 10 months return to ovulation on stopping (fat soluble → very slow metabolism)

Sterilisation

- Reversal is only 50% successful ⇒ see it as irreversible

- Tubal ligation has 1% failure (1:200) – 10 times worse than vasectomy and same as IUCDs
- Vasectomy – easier than tubal ligation, but takes up to 3 months before stored sperm used up. Need to be tested and have 2 sperm-free ejaculates. Has been discussion of ↑risk of prostate cancer – best evidence says no association.

Emergency Contraception

- Ask why: unprotected intercourse, condom broke, etc. If no condom, then check why. If indicated: ‘Are you worried about infection?’ and ‘Was it OK with you that it all happened the way it did’ [checking for non-consensual intercourse]
- Ask:
 - How long ago was sex?
 - LMP
 - Regular partner (→ ↓risk of STD)
 - Medications
 - Previously had an ECP – any side effects. Sometimes nausea +/- vomiting with Progesterone only ECP
 - Other conditions. Old Oestrogen + Progesterone ECPs required history of DVT and focal migraine
- If sex < 72 hours ago prescribe:
 - Nordiol 2+2/Antinaus 5mg (12 hours apart, few side effects) or
 - 2/Microval 25+25 (can have while breast feeding, may reduce breast milk for ~ 1 week)
- Discuss:
 - How to take it
 - Pregnancy test in three weeks
 - Ongoing contraception, other advice
- Emergency IUD: inserted within 120 hours of unprotected intercourse. Screen for STDs. Prophylactic cover if suspected

Suspicion of Abuse or Interpersonal Violence

- It is common and victims are high users of health services
- Epidemiology: 20% of women report sexual abuse before 16, full intercourse reported by 4%. Sexual abuse of boys is about 1/3 as common as for girls.
- Adult women: 25% report sexual abuse, 12% rape
- Men: 5% report sexual abuse, 3% rape (?under-reporting)
- 10 – 16 % of rapes reported to police
- Effects:
 - Acute and long term effects are related to age of victim, extent and duration of abuse, relationship with abuser and response of others
 - Acute effects: numbness, shock, disbelief, anxiety
 - Long-term effects: feelings of helplessness, depression, sleep disturbances, nightmares, flashbacks, guilt, self-blame, shame. Measurable long-term psychiatric sequelae in 25%
- What is patient's age:
 - < 14: all suspected cases should be referred to CYPFS, or if older but abuser still has access to young people. See also Child Abuse, page 656
 - 14 – 17 don't make a decision about what to do on your own ⇒ need to put caveats on confidentiality
- History questions (but don't introduce it in a crisis situation)
 - Suspect if physical injuries, chronic undiagnosed pelvic pain, heightened anxiety about an examination, STD's without being worried about health risks
 - They will be reluctant to discuss it
 - Physical: ‘have you ever been hit, slapped or shoved by a parent or partner. Ever had bruises or had to stay in bed...’
 - Sexual: Did anything sexually frightening happen to you as a child or young adult, have you ever been made to participate in sexual activity that made you feel uncomfortable. Was it your choice, or were you forced or coerced?
 - Psychological: Does your partner ever ignore you, call you names, make fun of you, threaten to leave you, punish the children when he is angry with you, are you fearful of anyone at the moment?

- Most helpful response is: being believed, being supported, not being blamed, being helped not to feel odd or alone

Rape/Non-Consensual Intercourse

- Rape: = sexual contact without consent (including consent under threat) which involves oral, genital or anal penetration, otherwise unlawful sexual contact
- Therapeutic role:
 - Recognise & treat physical injury
 - Attention to emotional trauma
 - Prevention of pregnancy – offer ECP. Legal requirement under the Contraception, Sterilisation and Abortion Act.
 - Check for infection (NB incubation of chlamydia is 21 days) and offer prophylaxis (but may interfere with ECP – do it after)
 - Referral to support services
 - If not sure about making a police complaint, bring in crisis counselling team
 - Victim compensation – inform re ACC entitlement
- Forensic role:
 - When did it happen: If less than 7 days then may be forensic requirements. If very recent then nil-by-mouth and collect all urine and toilet paper until forensic examination. Ring forensic specialist (DSAC = Doctors for Sexual Abuse Care)
 - Keep detailed records at the time of examination
 - Forensic specialist will do genital exam, blood tests, urine (drug screen), colposcopy (for genital injury), finger nail scrapings, etc and appear as expert witness
- Supportive role:
 - Communicate empathy: ‘that sounded really unpleasant for you’
 - ‘You are safe now’ (don’t say if not true)
 - Reinforce ‘It’s not your fault’ – victims blame themselves
- Follow-up at 1 week, 1 month and 3 months (pregnancy, HIV test, Hep B and C, Syphilis)

Infertility

- = Inability to establish a pregnancy within a year of unprotected intercourse or > 2 consecutive miscarriages or still births
- Normal fecundability = 25% per month, 85% per year, 90-95% per 2 years
- Incidence – approx 10% of couples
- Aetiology:
 - Male factors: 30%
 - Idiopathic/unexplained: 20%
 - Ovulatory: 10%
 - Tubal: 10%
- History:
 - Male: Previous surgery (eg hernia), undescended testes, mumps, etc
 - Female: surgery, menstrual history, BMI, symptoms of endocrine disorders, nasty polyps, PID, ectopic pregnancy, nasty appendicitis
 - Both: general medical and reproductive history, smoking, medications, family history
- Exam: include general assessment of endocrine disorders: PRL (\rightarrow Galactorrhoea), thyroid disorders (goitre, etc), Polycystic ovary (\rightarrow hirsutism, obese, etc)
- Investigations:
 - Male: semen analysis, sperm antibodies, Plasma FSH (primary or secondary testicular failure), androgen deficiency, testicular biopsy
 - Female:
 - Possible causes: Endometriosis, stress/anorexia/exercise, early menopause, PCO, thyroid, ↑PRL
 - Ovulation: if regular menstruation then ovulation likely. Only proof is laproscopic visualisation – impractical. Can measure temperature, progesterone levels, etc
 - Test HCG, TSH, PRL, Oestrogen (day 2), progesterone (day 21) for 3 cycles to check for consistent ovulation
 - Post-coital test of cervical mucus
 - Pelvic assessment: US, contrast x rays, etc

- Management:
 - Induce ovulation: risk of multiple pregnancy, also narrow TI. Anovulatory cycles: treat with Clomifene – stimulates ovulation but risk of multiple pregnancy
 - IVF (also better for tubal blockage than surgical repair). 1 in 3 have live birth.
 - Oligospermia: intracytoplasmic sperm injection, donor sperm, artificial insemination
- Lots of psychosocial implications of infertility
- Workup to point of diagnosis is funded. Criteria based funding for treatment
- Also prepare for pregnancy: take folate, do booking bloods, check rubella status and offer vaccination

Dyspareunia

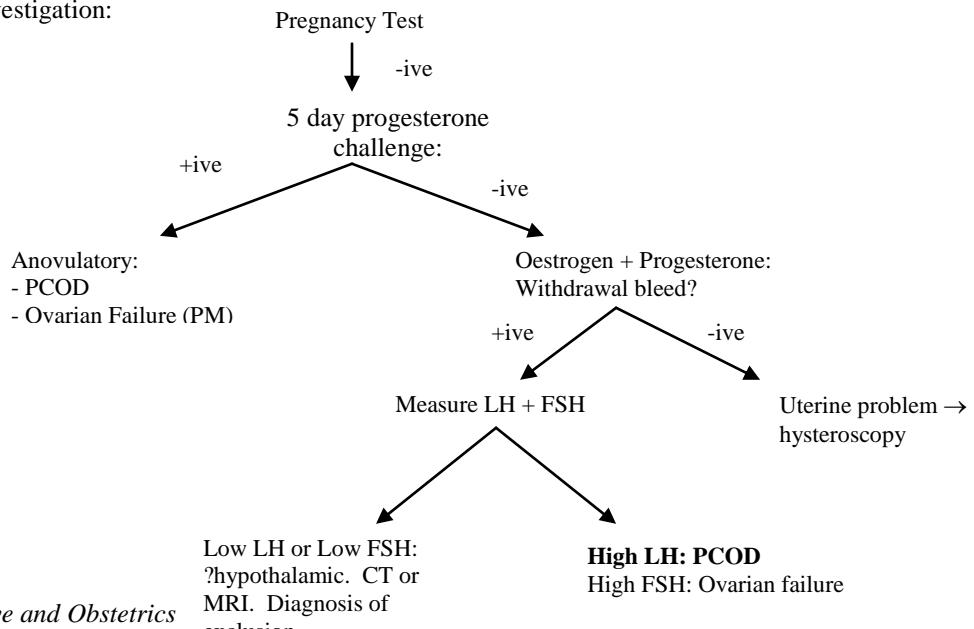
- = Pain with sex
- Causes:
 - Superficial pain: vulvitis (eg HSV), introital shrinkage (atrophy, scarring), vaginismus
 - Vaginal pain: post-menopausal atrophy, medication (eg antihistamines), arousal phase dysfunction
 - Deep-pain: pelvic disease (endometriosis, adenomyosis), shortened vaginal vault post-hysterectomy, retroverted uterus
- May be cycle of anticipation of pain → tense muscles and lack lubrication → further pain
- Treatment if no aetiology uncovered:
 - Lubricants
 - Oestrogen replacement
 - Position modification
 - Counselling
- Vaginismus: involuntary spasm of the levator ani muscle making penetration difficult. May be related to prior trauma/abuse. Pain-vaginismus-pain cycle develops. Treatment: behaviour modification, progressive vaginal dilatation

Menstrual Disorders

- Key distinction:
 - Ovulatory cycles: regular
 - Anovulatory cycles: irregular
- Also consider thyroid and ↑PRL

Amenorrhoea

- Primary amenorrhoea: failure to start menstruating. Investigate in a 16 year old or a 14 year old with no breast development. When did her mum start menstruating? Usually normal. Rarely Turner's syndrome or testicular feminisation
- Secondary amenorrhoea: when periods stop for > 6 months, except for pregnancy:
 - Hypothalamic-pituitary-ovarian causes common. Eg stress, anorexia, breast feeding, weight loss, ↑PRL, severe disease. Test with a 7-day progesterone challenge. If withdrawal bleed following, then there is enough oestrogen to produce an endometrium
 - Ovarian causes are uncommon: Polycystic ovarian syndrome, tumours, premature menopause
 - Hyperthyroidism → ↑oestrogen breakdown
 - Investigation:



- Oligomenorrhoea: infrequent periods: common in the young and the nearly menopausal. Consider polycystic ovary syndrome, rapid weight change, ↑PRL, hypothyroidism or primary oligomenorrhoea

Menorrhagia

- = Excessive blood loss (technically > 80ml lost/cycle – but hard to measure)
- Causes:
 - ?Hypothyroidism: cold intolerance, weight gain, constipation, goitre, etc
 - Younger: pregnancy, dysfunctional uterine bleeding (diagnosis of exclusion, no pelvic pathology, associated with anovulatory cycles. If young, may settle)
 - Older: IUCD, fibroids, endometriosis, adenomyosis, polyps, pelvic infection
 - Perimenopausal: ?endometrial carcinoma (especially if > 90Kg)
 - Haematological: low or dysfunctional platelets (not coagulopathy)
- Investigation:
 - βHCG: are they pregnant
 - FBC: anaemic?
 - Smear if not up-to-date
 - Menstrual calendar
 - Abdominal ultrasound
 - If age > 45, over 90 kg or infertile with heavy bleeding then transvaginal ultrasound and/or endometrial biopsy (pipelle) to test for endometrial cancer
 - Hysteroscopy and curettage for histology if irregular bleeding or ultrasound indicating polyps or fibroids
- Treatment if pathology known:
 - Anti-PGs (eg NSAIDs) as 1st line treatment
 - Progesterone during the follicular phase or CoC
 - Intra-uterine devices (eg Mirena)
 - Other drugs: Tranexamic acid, norethisterone, Danazol (bad side effects), etc,
 - Surgical options: endometrial ablation (problem with recurrence) or hysterectomy

Inter-menstrual bleeding

- May follow mid-cycle ↓ in oestrogen (ie with ovulation)
- Also cervical polyps, ectropion, carcinoma, cervicitis and vaginitis, IUCD, hormonal contraception (spotting)
- If post-coital, then ↑ suspicion of more serious pathology (eg cervical cancer)
- Appropriate to do an exam and smear – but it is NOT appropriate to rely on the smear result (false negatives, etc). Should act on clinical suspicion

Dysmenorrhoea

- = Painful periods, may be associated with sweating, tachycardia, headache:

	Primary	Secondary
Age	< 20	> 20
Onset of pain	With bleeding	Prior to bleeding
Duration	First 1 – 2 days of menses	Through out menses
Intensity	Begins with ovulatory cycles, remains constant	Begins at any time, progressively worsens
Aetiology	Probably PG-F2α mediated Pain without organ pathology	Cervical Stenosis Endometriosis Adenomyosis Pelvic Infection Fibroid/polyps Chronic sepsis (eg Chlamydia) Conditioned behaviour

- Treatment:

- Reassurance
- CoC: at least 3 month trial, combine with NSAIDs if necessary
- Progestogens: day 5 – 25
- PG inhibitors
- Exercise
- De-conditioning, eliminate secondary gains

Endometriosis

- = Ectopic endometrial tissue, histologically confirmed. Most often on ovaries and uterosacral ligaments
- Chronic and progressive: inflammation and local haemorrhage → fibrosis and scarring
- Incidence:
 - 10 – 15% of reproductive age. Patients usually in mid 30s – early 40s, nulliparous
 - Common in infertility and chronic pelvic pain
- Aetiology theories:
 - Retrograde menstruation → homologous grafts
 - Genetics: 7 fold risk if +ive family history. Usually earlier and more severe disease
- Symptoms: classic triad = pelvic pain, deep dyspareunia, dysmenorrhoea. Also irregular bleeding, infertility (scars fallopian tubes)
- On exam: tender, retroverted uterus
- Confirmation by laparoscopy. Red brown nodules on surface of ovaries and pelvic structures, and other sites (appendix, peritoneal scars, etc). Can develop large cysts, lined by endometrial stroma and glands and containing changed blood (chocolate cysts).
- Treatment:
 - Conservative (50% recurrence within 5 years): surgical removal (ablation or excision) of affected tissue and/or hormonal therapy:
 - Prostaglandin synthetase inhibitors treat pain (NSAIDs)
 - OCPs – promote inactivity of endometrial tissue
 - Progesterones – oral or depot
 - GnRH agonists – short course only due to bone loss
 - Danazol (testosterone derivative)
 - Laparoscopic resection or ablation of affected peritoneum
 - Radical: removal of pelvic organs

Fibroids

- Benign growths in myometrium (ie underneath the proliferative layer)
- Very common, especially in overweight and infertility
- Oestrogen → enlargement, so grow in pregnancy and shrink after menopause
- Aetiology unknown
- Symptoms: heavy/irregular bleeding, painful periods, urinary frequency, constipation
- Diagnosis: abdominal +/- vaginal ultrasound → hysteroscopy
- Treatment:
 - Medical:
 - GnRHa can shrink fibroids temporarily. Not for > 6 months, menopausal symptoms. Also Gestrinone and Danazol.
 - NSAIDs, Progesterone and HRT don't shrink fibroids
 - Surgical: Hysterectomy, hysteroscopic resection if small and submucosal, myomectomy (\uparrow risk of uterine rupture in subsequent pregnancy)

Adenomyosis

- = Growth of endometrial glands and stroma into the myometrium. Does not undergo cyclic changes and is not hormone responsive
- Symptoms: dysmenorrhoea, menorrhagia, deep dyspareunia
- Incidence: age 35 – 50, parous
- Exam: globular, enlarged uterus, most tender peri-menses
- Treatment: NSAIDs, OCPs, GnRH agonists, Hysterectomy

Premenstrual Syndrome (PMS)

- = Recurrence of symptoms, whether emotional or physical, occurring the pre-menstruum but with complete absence of symptoms in the post-menstruum. Severe symptoms in 5% of women
- DSM 4 has 'Premenstrual Dysphoric Disorder' as a research criteria
- Main symptoms:
 - Depression, irritability, tiredness, headache, bloating, breast tenderness.
 - Plus 150 others!
 - Classify as mild, moderate or severe on the basis of interference with daily function
 - Use of a symptom diary over 2 months is very valuable

- Diagnosis:
 - History
 - Exam to exclude gynaecological and endocrine disorders
 - Tests: rule out thyroid, PRL, secondary dysmenorrhoea (eg endometriosis)
- Differential:
 - Psychiatric: depression or anxiety with premenstrual exacerbation
 - Medical: anaemia, hypothyroidism, cancer, SLE, menopause if > 45, renal causes, polycystic ovary
- Management:
 - Education
 - Life-style changes: diet, exercise, ↓smoking
 - Psycho-therapy if psych history, for coping skills, or to manage secondary gains or conditioning
 - Drugs:
 - Suppression of ovulation. Eg with CoC – although this can give symptoms (eg depression, ache, etc)
 - Fluoxetine 20 mg only when symptoms occurring (30% remission, minimal side effects)
 - Debated remedies include evening primrose oil, Vitamin B6 (pyridoxine) in low dose (neuropathy in high dose)
 - Very high placebo rates
- Aetiology:
 - Multifactorial – includes biological, psychological and societal factors
 - Biological hypotheses include abnormal response to ovarian hormones, mineralocorticoid effects, prostaglandins, etc.

Post menopausal Bleeding (PMB)

- Bleeding > 1 year after the last period (check it is vaginal bleeding, not urethra or rectal)
- Causes:
 - Vaginitis (often atrophic): fragile → trauma, and ↓secretions → ↑infection
 - Foreign bodies (eg pessaries)
 - Endometrial or cervical polyps, endometrial fibroids (bleed a lot – leiomyoma, adenomyosis, hyperplasia)
 - Oestrogen withdrawal (HRT or ovarian tumour)
 - Carcinoma of the cervix
 - Endometrial cancer
- Distinguish from peri- or post-menopausal on HRT
- Investigation: Trans-vaginal US (looks at thickness of endometrium) and trans-abdominal US (finds other masses)
- If bleeding on non-cyclical HRT or intra-cyclical bleeding on cyclical HRT, be a bit more aggressive in investigation (HRT → slight ↑ risk of endometrial cancer)

Polycystic Ovary Syndrome (PCOS)

- Seek help for: infertility (anovulation), menstrual irregularity and androgen excess
- Symptoms: oligomenorrhoea, amenorrhoea, anovulation, infertility, hirsutism, acne, male pattern hair loss
- If rapid virilisation then look for tumour – not PCOS
- Associated with:
 - Obesity
 - Type 2 diabetes – insulin resistance → hyperinsulinaemia
 - Lipid abnormalities → vascular disease (eg 7 times risk of MI)
- Pathogenesis:
 - ?Primarily a disorder of LH hypersecretion
 - ↑Non-cyclical oestrogen (including from adrenal androgens and obesity) leads to:
 - ↑LH → ovarian hyperplasia → ↑androgens → perpetuates the cycle
 - ↓FH → ↓follicular maturation → ↓cyclical oestrogen → chronic anovulation → ↓progesterone → no menses
 - Hormonal cycling is disrupted and ovaries enlarged by follicles with have failed to rupture
- Investigations:
 - Serum total testosterone
 - Sex hormone binding globulin

- LH and FSH. Testosterone and LH high.
- Fasting HDL, LDL, cholesterol
- Glucose tolerance test (if pregnant do at beginning of pregnancy)
- Rarely: DHEAS for adrenal androgen tumour + 17-hydroxyprogesterone for congenital adrenal hyperplasia
- Treatment:
 - Diet and exercise → ↓ weight → ↓ peripheral oestrogen
 - Induce ovulation with Clomifene → ↑ FSH
 - Combined pill (Diane 35) to control bleeding and ↓ risks of unopposed oestrogen on endometrium
 - Metformin → ↑ insulin sensitivity, ↓ menstrual disturbance and ↑ ovulatory function
 - Prevention of risks of diabetes and ischaemic heart disease
 - Established facial hair won't go away when hormones corrects (require cosmetic treatment)
- Differential: Tumours of the ovary (eg granulosa and thecal cells) → chronic anovulation

Menopause

- Up to last period and 2 years following
- Primary ovarian failure → ↓ oestrogen feedback → ↑↑ FSH
- Continue contraception for one year following last period (eg PoP, IUCD, condoms)
- Usually age 50 – 51. Cycles start to slow from 47 – 48. Usually follows pattern of her mother.
- Factors affecting age:
 - CoC delays menopause (lots of eggs left over)
 - Earlier if chronic disease or toxins (eg radiation, chemo, etc)
- Signs:
 - Hot flushes, palpitations
 - Night sweats
 - Mood swings/depression
 - Vaginal atrophy → dyspareunia, post-coital bleeding
 - Urinary frequency/incontinence
- Test for high TSH if wanting to exclude thyroid and psychiatric problems

Hormone Replacement Therapy

- Replacing normal physiological dose of oestrogen (cf CoC which is much higher)
- Contraindications:
 - History of breast or endometrial cancer (not ovarian or cervical)
 - Undiagnosed vaginal bleeding
 - Liver disease (it's metabolised in the liver)
 - Pregnancy or breast-feeding!
 - Past PE
 - High cholesterol is NOT a contra-indication – it's protective (compared with OC dose of progesterone which is bad)
 - Smoking is NOT a contra-indication – it's protective
 - DVT is NOT a contra-indication (whereas OC dose of oestrogen is bad for clots)
- Benefits:
 - Especially good for those with hysterectomy, bilateral oophorectomy, ↑ risk of osteoporosis, IHD, ↑ cholesterol, DM, RA
 - Oestrogen effects: ↓ menopause symptoms, ↓ osteoporosis, ↓ CV disease (↓ LDL, ↑ HDL, vasodilates coronary arteries)
 - Progesterone effects: ↓ risk of endometrial cancer (if they have a uterus) by preventing proliferation of endometrium by unopposed oestrogen
 - ??Protective against colon cancer and Alzheimer's
- Side-effects: ↑ weight, PMS, cholestasis, vomiting
- Risks:
 - Minimal breast and ovarian cancer risk if taken for less than 5 years
 - Gallbladder disease
 - If severe heart disease then slightly ↑ risk of CV problems in 1st years

- Types:
 - Cyclical: continuous oestrogen, progesterone for any 10 days per cycle (with bleeding 2 – 3 days after its finished). Good if immediately post-menopausal – cycle them for a while and if no break through bleeding then → continuous HRT after a year
 - Non-cyclical: Continuous oestrogen and progesterone. No period as oestrogen and progesterone oppose each other → stable endothelium. Don't start until after menopause. Ovary may still be 'surging' from time to time → break through bleeding that you've got to investigate

Chronic Pelvic Pain (CPP)

- = Pelvis pain present for 6 months or longer. Can be intermittent (eg related to menses or intercourse) or continuous
- Differential:
 - Gynaecological: dysmenorrhoea, endometriosis, adenomyosis, pelvic adhesions, PID, uterine prolapse, vaginitis, pelvic congestion (engorgement of pelvic vasculature – ie varicose veins), pelvic relaxation (trauma of pregnancy etc)
 - Non-gynaecologic: UTI, interstitial cystitis, IBS, diverticular disease, musculo-skeletal disorders
 - Psychosocial: psychosomatic, abuse/rape, drug seeking, attention seeking
- Exam:
 - External genitalia, mono-manual (eg evidence of spasm), bi-manual, recto-vaginal (nodularity over uterosacral ligaments ⇒ endometriosis), speculum (eg discharge, cervical erythema)
 - Musculo-skeletal exam: tenderness over lumbar, lower thoracic muscles, strength
- Investigations:
 - Always: cultures, FBC, urine culture and analysis, US, pap smear
 - If indicated: pregnancy, GI and GU workup, psych evaluation, laparoscopy (if suspicious masses, other physical findings, acute abdomen, if for reassurance then wait a while first)
- Treatment:
 - Drugs: NSAIDs, PG-inhibitors, ?antibiotics, OCP for at least 3 months
 - GI: diet changes, stool softeners, bulking agents
 - Exercise

Pelvic Mass

- History: pain, bleeding, urinary and bowel symptoms, constitutional symptoms (weight loss, night sweats, etc)
- Exam: shape, consistency, mobility, etc
- Where:
 - Physiological: full bladder, flatus, faeces, pregnancy, obesity
 - Congenital: uterine anomaly, pelvic or polycystic kidney
 - Trauma: rectus abdominis haematoma
 - Infective: pyosalpinx, pelvic abscess, diverticulitis, TB peritonitis, lymph nodes
 - Neoplastic: fibroids, tumours of colon, rectum cervix or endometrium, ascites, retroperitoneal tumour, mesenteric cyst
 - Hormonal: non-neoplastic cysts
 - Mechanical: Hydronephrosis
 - Pregnancy associated: pregnancy in uterine horn or ectopic, trophoblastic disease, corpus luteum of pregnancy
- Investigations:
 - Pregnancy test
 - US
 - Ca125
 - ESR, FBC
 - Laparoscopy, colonoscopy

Vulval Lesions

- Non-neoplastic epithelial disorders:
 - *Lichen Sclerosis*:
 - 1/3 of lesions, commonest after menopause
 - Pruritic, affecting any part of the vulva
 - Multiple irregular white patches, shiny wrinkled atrophic skin
 - ↑ Risk of SCC

- Microscopy: subepithelial homogenous collagen + band of lymphocytes
- Autoimmune aetiology → treatment with steroids
- *Squamous Hyperplasia*:
 - Non specific thickening of the epithelium + inflammatory reaction below the BM: acanthosis, hyperkeratosis
 - Non specific diagnosis
- Other dermatoses: Lichen simplex chronicus, spongiotic dermatitis (contact dermatitis eg perfumed toilet paper), psoriasis, lichen planus
- *Vulval Intraepithelial Neoplasia (VIN)*:
 - Often multi-focal white-pink-red raised lesions which itch/burn/asymptomatic
 - Preinvasive dysplastic squamous lesions
 - Dysplasia is graded VIN1, VIN2, VIN3
 - Untreated 7/8 progress to SCC (unlike CIN)
 - Risk factors similar to cervical carcinoma
 - 60% have lesions in other areas
- *Squamous Cell Carcinoma*:
 - 90% of vulval cancer and 5% of gynae cancer
 - Two types:
 - Elderly women (70+): 65%, related to Lichen Sclerosis & squamous hyperplasia, well differentiated – islands of invading cells
 - Younger women (40+): 35%, related to HPV, Cervical cancer risk factors, poorly differentiated
 - Raised white warty mass
 - Micro: resembles SCC at other sites
 - Often present late
 - Prognosis depends on stage. Factors in order of importance are:
 - Lymph node metastasis
 - Depth of invasion
 - Size
- See also Non-Sexually Transmitted Genital Skin Lesions, page 386

Cervical Cancer

- Reference: Cervical Screening, Information for Health Professionals, National Cervical Screening Programme, Health Funding Authority, October 1998

Epidemiology

- In NZ, about 200 new cases per year, 70 – 80 deaths (⇒ relatively rare compared with other cancers)
- One in 97 women can expect to get it before 75
- 75% of cases and 80% deaths are over 35, but CIN lesions can develop young (ie many woman coming for colposcopy after abnormal smears are 25 – 30).

Aetiology

- Human Papilloma Virus (HPV):
 - HPV 6, 11: condyloma accuminatum
 - HPV 16 or 18: Genital dysplasia. Is a necessary but not sufficient condition for cervical cancer
 - Koilocytes: HPV infected keratinocytes with a perinuclear halo. Episomal viral DNA
 - Dysplasia: pleomorphic, hyperchromatic mitotically active, high nuclear/cytoplasmic ratio. Integrated DNA (Kettle fry nuclei)
- HPV Carcinogenesis:
 - Not typical mechanisms
 - E6 binds to p53 (tumour suppressor and accelerates its degradation)
 - E7 binds to RB displacing transcription factors usually sequestered by RB
- Other risk factors:
 - Early age at first intercourse
 - Multiple sexual partners
 - High risk male partners
 - Smoking
 - Herpes
 - Immunosuppression

- Occurs in the transformation zone: junction in the endocervix between squamous cells of the vagina and columnar cells of the uterus. Completes development at age 18 – 20, shifting into the endocervix. Previously in the exocervix and more vulnerable to damage/infection ⇒ significance of age at first intercourse

Classification

- 3 grading systems:

	Histology	Cytology
Mild dysplasia	CIN1	LSIL
Moderate Dysplasia	CIN2	HSIL
Severe Dysplasia	CIN3	HSIL
Carcinoma-in-situ	CIN3	HSIL

- Low grade changes: Low Grade Squamous Intraepithelial Lesion (LSIL) (=CIN1 – Cervical intraepithelial neoplasia). More likely to be HPV types 6 & 11). Nucleus is slightly enlarged and irregular. In bottom third of cells on top of base membrane in transformation zone. If found on screening → more regular smears. 50 – 60% return to normal
- High Grade Changes: HSIL (covers CIN 2 and 3/CIN – carcinoma-in-situ. More likely to be HPV 16 & 18). Nucleus of every cell is very enlarged and irregular in shape. High nuclear:cytoplasmic ratio. Affected cells right to surface. If found on screening → refer for colposcopy. Treated the same but CIN3 more likely to progress than CIN2
- Invasive cancer: basement membrane has been breached. Can get glandular extension in CIN3 – metaplasia down glands – but still not invasive as the BM is not breached

Progression

- Cervical Dysplasia: grade depends on the proportion of the epithelium occupied by malignant cells
- Cervical Carcinoma:
 - Micro: islands of infiltrating neoplastic squamous cells that may show keratinisation
 - Outcome: depends on stage
 - Size and depth of invasion. > 10 mm invasion → poorer outcome
 - Lymph node involvement → poor outcome
 - Stage 1: confined to cervix. 90 – 95% 5 year survival
 - Stage 3: lymph node positive: 30% 5 year survival
- Cervical glandular neoplasia:
 - Also HPV related, but much less common than cervical squamous carcinoma (which has a higher rate of replication)
 - Invasive adenocarcinoma has infiltrating neoplastic glands
 - Comprises 20% of tumours in a screened population vs 5% in unscreened

Cervical Screening

- Pap smears collect exfoliated cells from the cervix
- Currently reported on the Bethesda system which divides dysplasia into LGSIL, HGSIL and ASCUS (Atypical squamous cells of unknown significance – not sure whether they're dysplastic or reactive. Some will be CIN3 so still need follow-up)
- Procedure:
 - Best done mid-cycle (↓blood and ↓bacteria which are causes of cytolysis)
 - Explain first. Ask about LMP, abnormal bleeding, post-coital bleeding, abnormal discharge, if pregnant, and previous smear history and experiences
 - Patient Education: discuss feelings about having a smear, emphasise preventative nature, explain what cervix is, show equipment
 - Ensure screen/curtain for patient and sheet
 - Label slides first
 - Either:
 - Spatula** first, one full turn, and if poor endocervical sample follow with **brush** (only turn one turn otherwise bleeding → obscures sample) and use a second slide for the brush.
 - Broom** does both well (sample of choice for all age groups) – turn 5 times and wipe both sides once down slide. Thin prep: cells mixed up and rubbish removed → better reading. Can't use wooden spatula.

- Putting on slide: wipe spatula once, roll brush (scrubbing it around lyses cells). Fix quickly – within one second – as drying causes distortion of cells. Fix either in 95% ethyl alcohol for 20 - 30 minutes or cytofix sprayed from 20 – 30 cms.
- Data on lab form includes LMP and clinical details.
- Biggest cause of ↓ sensitivity is poor sampling. Smears can be unsatisfactory if blood, inflammatory cells or lubricant present. Smears taken 4 – 5 days prior to the next period may show cytolysis (cellular degeneration due to ↑ bacilli)

Relationship between screening results and lesions

- From OHCS, p 34:

	Papanicolaou class	Histology
1	Normal	0.1% CIN II – III
2	Inflammatory	6% CIN II – III
	Mild Atypia	20 – 37% CIN II – III
3	Mild/Moderate dyskaryosis	50 – 75% CIN II – III
4	Severe dyskaryosis	80 – 90% CIN II – III
	Malignant cells	5% invasion
5	Invasion suspected	50% invasion
	Abnormal glandular cells	?Adenocarcinoma

- NZ Protocol:
 - 3 yearly screening should be offered to all women aged 20 – 69 years who have been sexually active. Can stop if > 5 years with no sex (this bit not in the guideline)
 - Screening should be yearly for 2 years from 20 (some advocate starting earlier if > 2 years since commencing regular sex – but as cancer in this age group is very uncommon, it's not good screening practice. If you think cancer is a possibility, you shouldn't use a screening test to diagnose it)

- Normal or benign/reactive changes:

Satisfactory	Previously normal	Smear in 3 years
	First smear, or more than 5 years since last smear	Smear in 1 year
Satisfactory but limited	Previous abnormal smears	See below
	Previously normal	Smear in 1 year
	First smear, or more than 5 years since last smear	Smear in 1 year
	Abnormal smear in last 5 years	Smear in 6 months
Unsatisfactory smear		Smear in 1 – 3 months

- Abnormal:

CIN1 or HPV	Previous normal smear	Smear in 6 months
	Previous abnormal smear	Smear in 6 months, if normal then 2 * 1 year, if abnormal then colposcopy
CIN 2 or 3 → Colposcopy	If LSIL or less	Smears at 6 months, 1 year, 1 year, 3 yearly, if abnormal then colposcopy
	If HSIL	Smear at 6 months then annual until 70, if abnormal then colposcopy

Effectiveness of Screening

- Sensitivity of a single smear is 80% for low and high grade lesions (ie not sufficient for diagnosis, only for screening)
- PPV of HGSIL cytology report: 30 – 40%
- NPV of a normal smear is 80% ⇒ if abnormal appearing cervix (lesion with raised edge, nodular feel, hard, bleeds when touched) or persistent abnormal bleeding they need a colposcopy not a smear: DON'T RELY ON THE SMEAR
- Maximum prevention: 91-92 % of squamous cancers with 3 yearly screening. ↑ to 92 – 93% with annual screening. ↓ to 87% with 5 yearly screening

- Less than 100% because of:
 - Less than 100% enrolment
 - False negatives in sampling (eg a lesion is more likely to bleed and compromise the sample)
 - False negatives in laboratory diagnosis
 - Interval cancers: minimum time from infection to invasive is ~ 18 months. Normal is ~ 10 to 15 years
- Success rate for adequate treatment of pre-cancers is 98 – 100%
- Women most likely to get cervical cancer are those not regularly screened
- Much less effective at glandular lesions: clinical suspicion should overrule a ‘normal’ smear

Other Cancers

Ovarian cancer

- Risk factors: nulliparity, infertility, early menarche, family history, no past pill use
- Presentation:
 - 75% asymptomatic until advanced
 - Swelling with palpable mass
 - Pressure effects (eg on bladder)
 - Infarction, haemorrhage, peritonism
 - Ascites
 - Torsion
 - Endocrine: virilisation, menstrual irregularity, PMB
- Lower incidence than endometrial cancer, but higher death rate due to late presentation
- 5 Yearly survival ~ 30 – 35% (varies from 80 – 100% for FIGO I to 5 – 10% for FIGO IIIC/IV)
- Types:
 - Epithelium: 70%
 - Benign (60%): younger – serous cystadenoma, mucinous cystadenoma. If cysts have smooth internal epithelium likely to be benign
 - Borderline (20%): mucinous tumour of borderline malignancy. 6% recurrence (but still treatable) so need long term follow-up
 - Malignant (20%): serous cystadenocarcinoma
 - Ovum: 20%
 - Dermoid cyst (teratoma)
 - Occur in children and young women, in contrast to epithelial tumours
 - Commonest is benign, but in young children they are often malignant
 - Micro: variety of mature cell types: skin, gut, neural tissue, etc
 - Others: 5%
 - Stroma: lymphoma, fibroma
 - Granulosa cell tumour → ↑oestrogen → amenorrhoea and breakthrough bleeding
 - Thecal cell tumour → ↑androgen → infertile, hirsutism, amenorrhoea
- Investigations: Ca125, FBC, electrolytes, LFTs, US + CT (for mets or possible primary elsewhere)
- Should identify and screen those with high risk – those with genetic tendency (ie BRCA1, BRCA2, HPNCC). If family history then screen with US plus CA125 – more informative together. NB ↑ lead time bias
- Treatment: Surgery for staging +/- debulking, chemo (usually platinum)
- Other ovarian cysts:
 - Present with mass effects of torsion:
 - Follicular cyst
 - Corpus luteum cyst
 - Polycystic ovaries
 - Endometriosis

Endometrial Neoplasia

- Most common gynaecological cancer, but early presentation → better prognosis
- Endometrial hyperplasia:
 - Simple hyperplasia: cystic glands with pseudostratified mitotically active cells. No atypia, minimal risk of carcinoma
 - Complex hyperplasia: More crowded gland with budding and infolding. With atypia, 5% progress to carcinoma

- Complex hyperplasia with atypia: crowded, folded gland in which the lining cells are pleomorphic with loss of polarity and increased nuclear cytoplasmic ratio. > 25% progress to carcinoma
- Endometrial polyps:
 - Most are hyperplastic polyps
 - Often seen with generalised hyperplasia
 - Due to an area responding to oestrogen but resistant to progesterone
 - Micro: a polypoid collection of cystic hyperplastic glands in a fibrotic stroma
- Endometrial Cancer:
 - Presentation: irregular PV bleeding, often post menopausal
 - Risk factors: obesity, nulliparity, diabetes, unopposed oestrogen therapy, pelvic irradiation, endogenous unopposed oestrogen (functioning ovarian tumour, anovulatory cycles, fat), family history for breast, ovarian or colon cancer
 - Peak age 55 - 60
 - Investigate endometrial thickness with trans-cervical ultrasound:
 - Reproductive endometrium: 0.5 – 1.5 cm
 - Menopausal endometrium: < 5 mm. If bleeding, repeat US in 4 – 6 months and look for change
 - If menopausal and 5 – 9mm, do endometrial sample. 90% are normal proliferative endometrium. 5% are atypical (pre-cancerous), 5% are carcinoma
 - If > 9 mm, straight to D&C to get good endometrial sample (high suspicion of cancer). Not hysteroscopy (can force malignant cells into the peritoneum)
 - Macro: fungating mass in the fundus
 - Micro: adenocarcinoma
 - Treatment: hysterectomy and oophorectomy + chemo and radiotherapy
 - Prognosis:
 - Stage 1: invade wall, 90% 5 year survival
 - Stage 2: invade cervix, 50% 5 year survival
 - Stage 3: lymph nodes, 20% 5 year survival

Obstetrics

History and Antenatal Booking

- Always assume a woman is pregnant until proven otherwise, always assume a pregnancy is ectopic and the mother has pre-eclampsia until proven otherwise (these are the common dangerous and treatable conditions)
- Objectives of antenatal care:
 - Assessment and monitoring of maternal and fetal well-being
 - Preparing woman and family for childbirth
 - Preparing woman and family for parenthood
- Introduction Data:
 - Age: NB ‘Old’ at 35:
 - Hypertension/diabetes/DVT more common
 - Down’s: Past aged 35 risk of Down Syndrome > risk of amnio (approx 1 in 200)
 - Gravidity + Parity: Eg: G4P2 (+TOP + SAB). SAB = Spontaneous Abortion.
 - LMP – date of first day of bleeding in last period. Cycles regular? How long?
 - +/- Martial status
- History of current pregnancy – if yes to any then focused questions
 - Due date = LMP + 7 days + 9 months (Naegele’s rule), if 4 weekly cycle. If 6 weekly cycle, add 2 weeks (ovulation set by end of cycle not beginning)
 - Date it well. Management decisions later in pregnancy depend on dates being accurate. U/S more accurate early on ⇒ get accurate dates early on:
 - 1st trimester (< 12 weeks) accurate +/- 5 days
 - 2nd trimester (12 – 24ish weeks) accurate +/- 10 days
 - 3rd trimester (24+ weeks) accurate +/- 2 – 3 weeks
 - Morning sickness
 - Contractions/pain
 - Bleeding
 - Discharge/leakage (rupture of membranes)

- Foetal movements (from 18 – 20 weeks)
 - Urinary symptoms
- Past Obstetric History: For each pregnancy:
 - When was it
 - If TOP then:
 - How many weeks. If 6 – 8 then likely to be choice. If after first trimester maternal or congenital problem more likely so need to ask the reason for the TOP
 - Any problems (bleeding, infection, etc)
 - Antenatal problems/complications: hypertension, diabetes, PTL (Pre-term labour), medical problems
 - When did you deliver (how close to your due dates were you)? If pre-term then ↑ risk this time. Was there a reason?
 - How delivered? If caesarean need to check surgical report for type of incision. If it was low transverse can trial labour, if vertical then not. Skin incision not reliable indicator.
 - Weight of baby: big → ?diabetes (were they screened for diabetes – they will remember the sugar load), small → ?smoking or growth problem
 - Post partum bleeding, infection, depression
 - Breast feed, if so how did it go
 - How's the baby now?
- Past Gynaecological History. If indicated. See History, page 338
 - Actively treat any infection
 - Any chronic infections (eg Herpes)
 - Polycystic ovaries, uterine abnormality or surgery → ↑ risk
 - Gynaecological cancer: pregnancy hormones may exacerbate the disease
 - Contraceptive history – talk about restarting after pregnancy
 - Smear history: last smear date, any abnormal
- Past Medical and Surgical History (and maybe very brief systems review):
 - History of hypertension (any signs of renal disease?), DM, heart disease, asthma, epilepsy, RF, bleeding tendency, clots, previous STIs, TB, Hep B, gynaecological problems, kidney disease, clinical depression, autoimmune disease, thyroid
 - Previous surgery
- Medications:
 - See also Pharmacology of Pregnancy and Breast Feeding, page 528
 - Remember vitamins and non-prescription meds. Vitamin tablets not recommended in pregnancy (OHCS, p 95).
 - On folate (should be from before conception to 13 weeks)
 - Allergies
- Family History:
 - As for medical history
 - Clotting problems/DVT
 - Hereditary anaemias: Thalassemia (Mediteranian), Sickle Cell Anaemia (African)
 - Birth/Congenital defects (including congenital dislocation of hips)
 - Multiple births
 - Sister or mother with fertility or pregnancy problems (HT, miscarriages, DM, premature labour)
- Social History (key element in determining pregnancy outcome):
 - Adopted
 - Marital/relationship status, subject to domestic abuse
 - Support system
 - Cigarette, alcohol and recreational drug use
 - Occupation. Interested in exposures. Also stay away from high impact activity and keep HR < 140 (→ ↓placenta perfusion)
 - Financial well-being
 - Low socio-economic status → ↑ pregnancy complications (eg poor nutrition, lack of antenatal care, etc)
 - Enquire about anxieties, etc
- Offer advice on:
 - Questions or concerns (especially if first pregnancy or previous miscarriage)
 - Ante-natal screening

- Ante-natal classes
- Dental check-up
- Smoking and alcohol
- Diet, including folate, iron, listeria (nothing from the Deli unless it's piping hot, no imported soft cheeses - unpasturised)
- Morning sickness: keep glucose up (ie morning barley sugar)
- Rest
- Knowledge of social security benefits
- Mild exercise
- Intercourse OK if there is no vaginal bleeding
-
- Pregnancy write-up: [Name] is a [age] year old G_P_ LMP (date) EDD (estimated date of delivery)/EDC (estimated date of confinement) at _ weeks by [LMP or US at _ weeks] who presents for/complaining of etc.... Her prenatal course has been uncomplicated/complicated by.... Should also include (gestation dependent):
 - Contractions, abdominal pain
 - Bleeding
 - Rupture of membranes – discharge or leakage
 - Foetal movement – 1st baby about 20 weeks, 2nd baby maybe as early as 18 weeks

Booking Exam and Investigations

- Exam:
 - Pulse, blood pressure
 - Weight and height → BMI
 - Signs of thyroid disease
 - Signs of anaemia
 - Heart and lungs (eg wheeze, mid systolic murmur common, pan systolic and diastolic abnormal)
 - Breast exam, including nipples
 - Abdominal (masses, large liver, etc)
 - Oedema
 - Varicose veins
 - Fundal height
 - Fetal Heart rate by monitor (if old enough)
 - Vaginal
 - Bi-manual – uterus size consistent with dates and no adnexal masses. Uterus becomes an abdominal organ (rather than pelvic) at 12 weeks
- Tests:
 - Blood:
 - FBC: check for anaemia
 - Blood group: check if RH –ive. If so, mark clearly in notes. Give Anti-D following birth or invasive procedure
 - RBC Antibodies (eg Anti-D, Anti-ABO, etc)
 - Serology:
 - Syphilis (VDRL): treat with course of penicillin IM
 - Hepatitis B: if +ive, test and immunise partner and close contacts. At birth give Hep B IgG and Hep B vaccine to baby (repeat at 1 and 6 months)
 - Rubella: If negative for Rubella and pregnant then NO vaccine (it's a live vaccine). Stay away from kids. If she gets sick, repeat serology 2 – 3 weeks later to see if it was Rubella. 70% fetuses affected in 1st trimester, drops to < 5% by 16 weeks.
 - MSU for protein, bacteria and glucose
 - High vaginal swab where indicated for chlamydia, gonorrhoea, bacterial vaginosis, candida, trichomoniasis, etc
 - If indicated:
 - Smear if not up-to date
 - Ultrasound if dates unsure (otherwise offer morphology at 18 weeks)
 - Tb if high risk (immigrant, family contact, etc)
 - Sickle cell anaemia if black
 - α-feta protein/triple test if at risk of Down

- HIV test if at risk
- If > 35 then offer amniocentesis
- Subsequent visits: see Assessment of Fetal Growth and Well-Being, page 359

Minor symptoms of Pregnancy

- Pregnancy testing: requires a few drops of urine, +ive from first day of missed period until week 20, false +ives low
- Early: amenorrhoea, nausea, vomiting, bladder irritability
- Nausea: At 20 weeks, 20% may still vomit. Reassure, small meals and ↓stress
- Headaches, palpitations and fainting due to peripheral dilation. Drink lots
- Urinary frequency (exclude UTI)
- Abdominal pain
- Breathlessness
- Constipation due to ↓motility. Give fibre and lots of fluid
- Reflux oesophagitis
- Backache in 3rd trimester
- Carpal tunnel syndrome (due to fluid retention)
- Itchy rashes
- Ankle oedema – almost universal. Exclude ↑BP and proteinuria (⇒ pre-eclampsia)
- Leg cramps

“At Risk” Pregnancies

- Adolescent Pregnancy (usually considered < 16):
 - Usually no problems with size of pelvis
 - Psychological and social problems: stability of relationship, financial (no DPB until 16), may conceal pregnancy or have poor access to care, if very young may involve incest → criminal offence, need ↑ support after birth
 - Obstetric problems:
 - Inaccurate dates
 - Compliance issues
 - Pre-diagnosis exposure to alcohol/drugs
 - Smoking
 - ↑Risk for pre-eclampsia (more likely to have less immunological tolerance to partner)
- Elderly Primagravid (> 35):
 - ↑Risk of chromosomal abnormality, twins, pre-eclampsia (more likely to have essential hypertension, SLE or renal disease), DVT, thyroid disease, gestational diabetes, labour problems
 - IVF pregnancy → ↑risk of prematurity, IUGR
 - ↑Risk of fibroids (which double in size in pregnancy) → malpresentation, outgrow blood supply (→ pain) but usually little problem to pregnancy
- Grand Multip (≥ 5 pregnancies)
 - Fe deficiency
 - Precipitate labour: can → uterine rupture due to ↑ efficiency
 - Post-partum: relaxes quickly → APH
 - Lie can be very unstable

Multiple Pregnancy

- Causes of large uterus for dates (in order of occurrence):
 - Incorrect date for LMP
 - Distended bladder
 - Multiple fetuses
 - Polyhydramnios
 - Adnexal mass
 - Large for gestational age fetus
 - Fetal macrosomia (in diabetes)
 - Hydatiform mole
- Dizygotic twins:
 - Baseline risk: 1 in 80 pregnancies. 1 in 40 if primary relative a dizygotic twin

- Siblings that happen to share the uterus at the same time: separate placentas, amnions, and chorions
- 2/3 of twins
- 7 – 11 per 1000 births
- Risk factors: > 35 years, high parity, ethnicity and assisted conception
- Monozygotic twins:
 - Family history has minimal risk for monozygotic
 - Splitting at two cell stage (< 5 days) gives separate placenta, amnion and chorion
 - Splitting at inner cell mass (5 – 10 days) gives common placenta and chorionic sac, but separate amnions (most common – 70%)
 - Splitting of inner cell mass at later, bilaminar disc stage gives common placenta, amnion and chorion
- Problems:
 - Cord entanglement: highest risk < 30 wks → occlusion and fetal death
 - Conjoined twins (1% of monozygotes): incomplete splitting of primitive node
 - Twin reversed arterial perfusion syndrome: one twin develops at the expense of the other
 - Fetus Papyraceus/Vanishing twin – death and subsequent reabsorption of one fetus
- Complications: all complication rates are increased
 - Maternal:
 - Pre-eclampsia: 3* risk
 - APH: 6% (4 – 5% in singleton), PPH: 10% (4 – 6 % in singleton)
 - Preterm labour: on average 3 weeks early
 - Mal-presentation: only 40% present cephalic/cephalic
 - Hypertension
 - Gestational Diabetes
 - Miscarriage
 - Iron and folate deficiency
 - Acute polyhydramnios
 - Fetal:
 - Fetal growth retardation (~500 g less than expected in 25%)
 - ↑Still births and infant mortality
 - ↑Congenital malformations, mental retardation and neurological damage
- Management:
 - More regular monitoring: eg hypertension and diabetes
 - Iron, folate supplementation
 - Introduction to multiple pregnancy support groups
 - Hospital delivery: obstetrician, midwife, 2* paediatrician, etc
 - Aim for vaginal delivery of first twin, syntocinon after delivery of first

Fetal Welfare

Assessment of Fetal Growth and Well-Being

- Clinical assessment. Key issue is serial measurement:
 - Mother:
 - Blood pressure
 - Maternal weight
 - Test urine from 20 weeks for albumin (ie proteinuria) and glucose
 - Oedema
 - Check Hb and Rh antibodies (eg at 28 weeks) and do glucose challenge
 - Baby:
 - Symphyseal-fundal height (SFH)
 - Indicator of weeks gestation – roughly 1 cm per week. Drops a bit at term
 - Measure from top of pubic bone to top of uterus
 - NB – can just palpate uterus on the abdomen at 12 weeks. At 20 weeks up to umbilicus
 - Lie and presentation from 32 weeks
 - Fetal heart: use Doppler (mum can hear it too). Normal is 110/120 to 160 bpm.
 - Fetal movements (from 19 – 20 weeks in primips, earlier in multipips): if no movement then asleep or sick. Awake foetuses are active

- OSCI tips:
 - First introduce yourself, wash hands, get sheet to cover legs
 - **Explain** what you're going to do
 - BP in sitting/semi-reclined position
 - Look for oedema – especially pre-tibial. Enquire about hands and face
 - **Inspect** abdomen for shape, size, scars, striae and linear nigra, symmetry. Is the baby transverse or longitudinal
 - Measure fundal height
 - Find poles to determine lie
 - Where is the back: Feel laterally (brace hand other side), then walk hands across.
 - Ask what position it was on last scan and ask where she's feeling movements
 - Pawlicks grip above symphysis then both hands to measure descent. Watch face for pain
- 20-week morphology scan. Fetal risk 0%. Operator dependent. Assesses:
 - Fetal number, lie and cardiac activity
 - Fetal anatomy: CNS, CVS, GIT, GU, musculoskeletal anomalies (eg neural tube)
 - Gestational age (BPD, head/abdomen circumference ratio, femur length)
 - Amount of amniotic fluid (poly or oligo-hydramnios)
 - Placental location (low lying?)
 - Pelvic pathology: fibroids, cysts, etc
 - Give reassurance: ↓parental anxiety
- Further investigations: Most have high false positives ⇒ interpret in light of clinical picture
 - Cardiotocography (CTG - fetal heart rate monitoring). See Cardiotocography (CTG) in Labour, page 371
 - Doppler ultrasound of blood flow in umbilical artery (not routine)
 - Ultrasound scan: fetal size (biparietal diameter, abdominal circumference, femur length), amniotic fluid estimation, assess fetal breathing (eg ↓ in hypoxia)
 - Biophysical Profile: Only if high risk. Score of fetal heart rate, breathing movements, fetal movement, fetal tone and amniotic fluid volume. Not often done in NZ

Prenatal diagnosis

- Reasons for prenatal diagnosis:
 - If an abnormality is detected, termination may be considered
 - Knowledge of an abnormality may give time to adjust/prepare
- For Down syndrome see Down Syndrome, page 581
- Screening tests (higher false +ive, especially if low risk women) – used to modify existing risks:
 - Fetal nuchal translucency (= nuchal fold): at 10 - 14 weeks, measure soft tissue thickening on posterior neck, normal < ~ 3 mm. ↑Thickness (adjusted for maternal and fetal age) associated with chromosomal abnormalities. Combine with other risk factors (eg age). Fetal risk 0%
 - Maternal serum screening (triple blood test – now quadruple test): at 15 – 17 weeks, measures AFP, HCG and free and bound oestriol. Serum levels, maternal age and gestational age are used to calculate the risk of neural tube defects and chromosomal abnormalities → classification as high risk (eg 1:50 for Down) or low risk (1:2700 for Down). Fetal risk 0%
- Diagnostic tests (higher false -ive):
 - Indications: positive results from screening, previous child affected by a congenital/genetic disorder or family history, maternal age > 35, maternal condition or medication with possible effect on baby
 - All introduce risk of Rh isoimmunisation ⇒ give anti-D afterwards if RH -ive
 - *Chorionic villous sampling* (CVS): from 10 weeks, trans-abdominal or trans-cervical. Karyotyped in 2 days, gene/enzyme analysis takes longer, 1 – 3% miscarriage. Can't detect neural tube defects. Complicated by maternal contamination or fetal mosaicism (~ 0.5%). If mosaic, skin cells in fetus closer to the babies karyotype than placental cells
 - *Amniocentesis*: from 14 weeks (10 – 13 weeks → 5% miscarriage). Culture amniotic cells for 2 – 3 weeks → detects chromosomal abnormalities and neural tube defects. Risk 0.5% miscarriage. Gold standard but late. Difficult if anterior placenta or oligohydramnios
 - *Cordocentesis* (Percutaneous umbilical blood sampling): from 18 weeks. Miscarriage rate of 1 – 3%. Rapid karyotyping – good for detection of fetal blood disorders and infection (eg rubella)

Fetal Growth Restriction (FGR)

- = Intra-uterine Growth Retardation (IUGR). Don't use this term in front of parents!

- = Failure to achieve full growth potential. Not quite the same as small for gestational age (< 10th percentile)
- Causes of ↓SFH: descent, changes in lie, IUGR, oligohydramnios
- Common cause of perinatal death (along with prematurity and congenital malformation)
- Associated with NIDDM, hypertension, heart and thyroid disease in later life
- Asymmetrical:
 - Chronic placental insufficiency – head preferentially protected
 - Occurs in maternal illness/smoking, multiple pregnancy, idiopathic
 - → ↓Abdominal circumference of the head, ↓amniotic fluid
- Symmetrical: Everything smaller due to eg congenital malformation, chromosome abnormalities, infections or toxins

Termination of Pregnancy (TOP)

- Crimes Act 1961:
 - Killing a child: child by definition is not a child until delivered
 - Killing an unborn child: prison term not exceeding 14 years
 - Unlawful to unlawfully procure an abortion for a woman
 - Section 187a: It is not unlawful to procure an abortion for a woman if:
 - Not more than 20 weeks gestation and either:
 - Continuing the pregnancy ‘would result in serious danger (not being danger normally attendant upon childbirth) to the life, or physical or mental health of the woman or girl
 - That there is a substantial risk that the child, if born, would be so physically or mentally abnormal as to be seriously handicapped
 - That the pregnancy is the result of intercourse between a parent and a child, a whole or half blood brother and sister, grandfather, is the result of sexual intercourse that is an offence against section 131(1) or the girl or woman is severely subnormal
 - If the woman is near the beginning or end of child bearing years, or if there is reasonable grounds to consider the pregnancy was the result of rape, then these factors may be taking into account (although are not sole grounds for termination)
 - More than 20 weeks, and the termination is ‘necessary to save the life of the woman or girl or to prevent serious permanent injury to her physical or mental health’
- Contraception, Sterilisation and Abortion Act 1977 specifies the process, not the criteria, for getting an abortion. Abortions must be certified by two certifying consultants. These people to be chosen by the Abortion supervisory committee, with a view to expeditious access by any woman seeking an abortion. Supervisory committee also appoints/approves counselling services
- Ethics:
 - Why is killing wrong:
 - Violates the moral integrity of the entity killed
 - It has negative consequences
 - Evidences moral flaws in the killer
 - Reasons for killing: to end suffering, to protect the innocent, lesser of two evils, to express societal condemnation
 - Different views of the moral status of the fetus:
 - Fetus has the same moral status: absence of a dividing line between a baby and a fetus does not show lack of difference
 - Fetus has no moral status: Is seeking an abortion for trivial reasons wrong?
 - Fetus has some moral status: As the fetus develops, reasons have to be increasingly weighty
- Cervical softening before surgical abortion: misoprostol
- Medical abortion: use of IU486/mifepristone

Complications of Early Pregnancy

Differential of early pain/bleeding

- 20% of women bleed in early pregnancy – it is never normal ⇒ investigate
- Obstetric causes: miscarriage, ectopic, trophoblastic disease
- Gynaecological causes: period, STI, cervical (eg polyps), vaginitis, endometriosis, ovarian cyst (may be functional → irregular cycles), PID
- Non-gynaecological: UTI, GI (eg haemorrhoids)
- Exam:

- CV, Resp, temp
- Abdominal: tenderness/guarding/rebound
- Pelvic exam:
 - Speculum: discharge, bleeding, swabs, os
 - Bimanual: mass, endometriosis (\rightarrow fixed, retroverted uterus and utero-sacral nodularity on PR), cervical motion tenderness (\Rightarrow ?PID)
- Investigations:
 - MSU, FBC
 - Blood type + Rhesus

Spontaneous abortion/Miscarriage

- = Loss of products of conception before the 20th week.
- 10 – 15% of recognised pregnancies. >75% in first trimester and due to fetal causes
- **Threatened abortion:** os is closed and fetus is viable (still has heart beat). Uterus right size for dates. 75% will settle. Associated with preterm delivery
- **Incomplete abortion:** cervix is dilating, more pain, heavier bleeding. Conservative treatment if < 13 weeks. If ↑ pain, ↑ bleeding or retained tissue on US then suction curettage. Ergometrine (uterine smooth muscle contractor) for severe bleeding
- **Complete abortion:** Products of conception expelled, bleeding stopped, cervix closed (don't confuse with threatened), uterus small for dates
- **Septic Abortion:** as for incomplete abortion + uterine and adnexal tenderness, purulent loss, pyrexia. Can lead to severe sepsis
- **Missed abortion:** Fetus dead but not expelled, uterus small for dates, confirmed by 2 US scans 7 days apart. Usually active management to remove fetus
- Causes:
 - None found – most common
 - Chromosomal abnormalities
 - Hormonal imbalance: eg failure of corpus luteum to produce enough progesterone
 - Maternal illness, abnormalities of the uterus (eg cervical incompetence), immunological factors
- **Recurrent miscarriage** = loss of 3 or more consecutive pregnancies, occurs in < 1%

Ectopic pregnancy

- = Any implantation outside the uterine cavity. > 95% in the fallopian tube
- 0.5 – 1 % of pregnancies. Fatal if untreated. Most common cause of death in 1st trimester
- Risk factors – anything slowing ovum's path to the uterus: salpingitis (eg PID), surgery, previous ectopic (recurrence in 10 – 20%), endometriosis, IUD
- Presentation:
 - Abdominal pain or bleeding in any sexually active woman
 - Usually around 8 weeks amenorrhoea, but may not have missed a period
 - Can present with acute rupture – sudden severe abdominal pain and shock
 - Shoulder tip pain due to blood in the peritoneum irritating the diaphragm
 - Cervical excitation
- Diagnosis:
 - β HCG – low for gestational age and rises slower than normal (normal doubling time is 2 days)
 - ?Quantitative β HCG: at 1500-2000 should see sac on trans-vaginal US, at 6000 should see sac on abdominal US
 - US can visualise in 2% of cases – key finding is empty uterus
 - Laparoscopy is gold standard
- Treatment: surgical or methotrexate (folate antagonist)

Trophoblastic disease

Partial Mole	Complete Mole	Choriocarcinoma
Triploid 69 XXX, 69 XXY (ie fertilised by 2 sperm)	46 XX, (46XY)	46
Normal and dilated villi – some initially have a fetus	Dilated villi with trophoblast proliferation	No villi. Atypical proliferating trophoblast
Little invasive potential	10% invasive, Choriocarcinoma 5%	Most have metastasised at diagnosis. 80% survival

- Complete or partial hydatidiform mole: abnormal placenta without/with a fetus. Placenta replaced by a mass of grape-like vesicles
- Choriocarcinoma: malignant invasion by trophoblastic cells – can arise years after a pregnancy
- 1 in 2000 pregnancies
- Risk factors: early or late maternal age, previous mole, previous multiple pregnancies
- Presentation:
 - Uterus large for dates in 50%
 - Vaginal bleeding +/- passage of grape-like villus
 - Early pre-eclampsia
 - Very high levels of HCG
 - Ground glass appearance on US and no fetus or absence of fetal movements/heart sounds

*Hyperemesis gravidarum**

- Rare (1 in 1000). ↑ Risk if young and primip
- Presents with inability to keep food or drink down, hypovolaemia, polyneuritis (↓ Vit B), liver and renal failure
- Admit to hospital. Rehydrate, exclude UTI, twins, and hydatidiform mole

Cardiovascular Problems in Pregnancy

- Common clinical findings in pregnancy: ↑ pulse volume, ↑ JVP pressure waves, ↑ heart size (apex beat displaced by approx 1 cm), loud first heart sound, 3rd heart sound, ejection systolic murmur up to grade 3/6 in 90% women, peripheral oedema
- Maternal mortality = 1 per 10,000 – most in puerperium (especially mitral problems → ↓ pulmonary flow → pulmonary oedema, especially during 3rd stage of labour due to sudden ↑ in blood volume as uterus contracts).
- Risk of heart failure, especially due to Rheumatic fever, congenital disease, Marfan's, prosthetic valves, given reduced functional reserve in pregnancy (ie further stresses an already stressed heart)
- Fetal mortality: usually little impact, except mums with cyanotic congenital heart disease
- History: breathlessness (although very common in pregnancy), syncope, arrhythmia
- ECG: T wave inversion in III, S-T changes and Q waves occur frequently. ECG best for arrhythmias, not structural problems (use echocardiogram)
- Management: avoid exacerbating factors: infection, hypertension, obesity, anaemia, arrhythmias, smoking etc. Multiple pregnancy → further 30% increase in CO which compromises function further
- Drug Treatment: digoxin, diuretic therapy, β blockers
- Labour: care not to fluid overload, monitor BP carefully (don't want it either up or down – care with aorto-caval compression and epidural).

Gestational Diabetes Mellitus (GDM)

- = Any degree of glucose intolerance with onset or first recognition during pregnancy
- For most it consists of mild glucose intolerance manifest during the 2nd or 3rd trimester and normalising following delivery
- Affects 4 – 8 % of all pregnancies (Indian women >> than European). Risk factors:
 - Maternal age > 35 years
 - Family history of diabetes
 - Previous macrosomia, unexplained still birth
 - Obesity
 - Glycosuria on two or more separate occasions. 20% of women have glucose in their urine ⇒ not a reliable indicator
- Associated with:
 - ↑ Morbidity for mother – 1.5 times risk of caesarean delivery
 - Increased risk of type 2 diabetes in the mother (up to 50% over next 10 years). ?Would have got it anyway. Also hypertension, hyperlipidaemia, etc.
 - ↑ 2.5 times morbidity for baby, including:
 - Large for gestational age, macrosomia (birth weight > 4000 gm – but most macrosomic babies' mothers have normal glucose tolerance)
 - ↑ Risk of inter-uterine fetal death (IUFD)
 - Possibly ↑ neonatal jaundice, polycythaemia, post-natal hypoglycaemia, prematurity – but not congenital malformations (unless IDDM mother)
 - But in general risks are low

- Is usually asymptomatic (ie no polyuria and thirst). Risk factors have low predictive power \Rightarrow universal screening usual
- NZ guidelines:
 - All women should be tested for glucose intolerance following a 50g glucose load between 24 and 28 weeks, blood sample 1 hour later. Normal < 7.8 . If very high risks (eg previous GDM) screen at 18 weeks as well
 - If failed screening test then formal test is 75g fasting load with samples at 0,1 and 2 hours. Normal is < 5.5 , < 11 and < 8.5 at 0,1 and 2 hours. If any *one* is abnormal then GDM.
 - See also Diagnosis of diabetes, page 94
- Exam: includes checks of eyes (retinopathy) and hands and legs (neuropathy), urine for protein
- Aetiology: \uparrow human placental lactogen (HPL, increases through pregnancy) $\rightarrow \uparrow$ insulin resistance $\rightarrow \uparrow$ insulin production. May unmask sub-clinical NIDDM.
- Management:
 - Diet and exercise (but don't calorie restrict them – ketosis is bad for babies)
 - Regular monitoring – home glucose monitoring and Hb A1C – normal is less than 6.5, under 8 acceptable. Aiming for pretty tight control
 - Insulin used if unable to control levels, or evidence of macrosomia. Stop once labour starts – requirements fall dramatically after delivery
 - Sulphonylureas and metformin not approved in pregnancy
 - $\rightarrow \downarrow$ Frequency of macrosomia but less clear effect on perinatal mortality and rate of caesarean section
 - Do GTT 6 weeks after delivery to check for type 1 or 2 diabetes
- IDDM:
 - Need to conceive when Hb A1C < 8 . Even if tightly controlled, 4 – 5% risk of congenital abnormalities (2* general population). Most common are neural tube and heart defects
 - Check for retinopathy at least twice during pregnancy
 - Get baseline renal function and ECG/Echo if cardiac problems
 - Usual insulin injections have shorter action \Rightarrow control harder. In early pregnancy, insulin requirements may reduce. Later they usually increase.
 - Usually induced before term

Hypertension in Pregnancy

Normal Changes in Blood Pressure

- Physiology:
 - \uparrow O₂ consumption from 300 to 350 ml per minute
 - \uparrow CO from 5 to 6.5 - 7 litres per minute due to \uparrow Stroke volume (10%) and \uparrow HR (15 bpm)
 - Peripheral resistance falls (due to hormonal changes)
 - \downarrow PCO₂ to 31 mm Hg to increase gradient for shifting CO₂ from fetus
 - \uparrow Blood volume by 40% from early pregnancy to delivery
 - \uparrow Ventilation
 - \uparrow Glomerular filtration $\rightarrow \uparrow$ urination
- During first and second trimesters, BP (especially diastolic) falls by 10 - 20 mmHg, return to booking BP by 3rd trimester (partly due to hypotension $\rightarrow \uparrow$ aldosterone)
- Venous distensibility + \uparrow venous pressure predispose to varicose veins

Essential Hypertension

- Present before pregnancy and commoner in older multiples
- If high blood pressure before 20 weeks, probably pre-existing hypertension
- Aim to keep BP $< 140/90$
- 5 * more likely to develop pre-eclampsia than normotensive women
- Watch for 'white-coat' hypertension

Pre-eclampsia

- = Pregnancy-induced hypertension with proteinuria +/- oedema
- = Toxaemia
- = Pre-eclampsic toxæmia (PET)
- = Gestational Hypertension

- Signs: > 20 weeks pregnant, oedema, proteinuria, ↑BP (\uparrow systolic by 20 - 25 or \uparrow diastolic by 15 over booking BP)
- If < 20 weeks then ?hydatiform mole
- Is asymptomatic \Rightarrow requires screening
- May recur in a subsequent pregnancy
- Risk factors:
 - Primiparity
 - New partner
 - Previous or family history of pre-eclampsia or eclampsia
 - Overweight
 - < 20 years or > 35 years
 - Multiple pregnancy (or anything else that \uparrow placenta size)
 - Renal disease, essential hypertension, diabetes
 - IVF
 - Autoimmune disease (eg SLE, anti-phospholipid syndrome)
- Presentations:
 - In ‘normal’ pregnancy (ie low risk) – PET is usually mild and late (eg from 37 weeks)
 - In ‘abnormal’ pregnancy, may begin from as early as 20 weeks and be severe
- Pathogenesis: Abnormal vascularisation of the placental decidua by the syncytiotrophoblast during the secondary invasion (~ 28 weeks). Arterial wall in placenta does not distend enough to allow sufficient blood flow to placenta in late pregnancy \rightarrow Mother doesn’t get the right pregnancy triggers from the placenta \rightarrow mother’s body doesn’t completely adapt to being pregnant
- Effects:
 - Mother doesn’t vasodilate sufficiently \rightarrow ↑BP, ↓plasma volume and ↑peripheral resistance
 - Generalised oedema eg face
 - Proteinuria is a late sign \Rightarrow renal involvement. Oliguria \Rightarrow renal failure
 - Serious signs (\rightarrow Urgent admission):
 - Signs of ↑ICP: headaches, vomiting, hyperreflexia, bilateral clonus
 - *Headache*, stomach pain, vomiting, ↑HR (ie mimics viral illness)
 - Sustained vasoconstriction \rightarrow ischaemia (eg *visual changes*, brain) and ↑clotting/DIC. Also affects liver (*RUQ pain*), kidneys
 - Placental abruption
 - Placental ischaemia
- Effects on fetus:
 - Asymmetric growth retardation (brain preferentially preserved)
 - If untreated \rightarrow symmetric growth retardation (if this occurs on its own then pre-existing fetal abnormality)
 - ↓Fetal movements, fetal respiratory effort and ↓amniotic fluid
- Assessment:
 - Baby: CTG and US
 - Mum:
 - Most important of the following are platelets and uric acid
 - FBC:
 - Either ↑Hb (haemoconcentration secondary to oedema) or ↓Hb (haemolysis secondary to DIC)
 - ↓Platelets – adhering to damaged capillary endothelium
 - Liver function tests: ↑AST/ALT (not ALP – that’s produced by the placenta). NB exclude acute fatty liver of pregnancy
 - Creatinine and Uric Acid: ↑ due to ↓renal flow. If bad then 24 hour urine to check for oliguria/renal failure
 - Coagulation: ↓fibrinogen due to DIC
- Treatment:
 - Low dose aspirin \rightarrow pregnancy runs closer to term (controversial)
 - Mild: monitor BP and fetus; rest up (but not bed rest). If problems and > 37/40 then induce
 - Moderate: (eg BP of 140/90 but stable):
 - Labetalol (want β 2 activity without any α activity). Contraindicated in asthma
 - Methyldopa (causes depression etc but safe for the fetus)
 - Nifedipine (other Ca blockers cause fetal malformations)

- Severe: Hydralazine IV (\downarrow BP). Aspirin (blocks thromboxane production → preferentially make prostacyclin), antihypertensives, anticonvulsant prophylaxis (Magnesium sulphate). Have to stabilise before delivery
- Delivery is the only cure (although > half of fits occur post partum). Antihypertensives only mask the disease. Diuretics contra-indicated. May have serious illness with only mild proteinuria (1+). Usually resolves over 10 days.
- Deliver now if \downarrow platelets, signs of renal failure, unstable BP etc (ie signs of serious disease), or if at term (>37 weeks)

Eclampsia

- 1 in 2000 pregnancies
- Major cause of maternal and fetal morbidity/mortality
- Is unpredictable. BP is not a good marker of disease
- Generalised seizures (eclampsia) – treat with Magnesium sulphate (better than diazepam)
- Death from stroke (most common), liver, kidney or heart failure

Other Complications of Later Pregnancy

- Key complications: preterm labour, pre-eclampsia and small babies

Antepartum haemorrhage (APH)

- Any bleeding from the genital tract between 20th week and delivery
- Differential diagnosis:
 - Placenta praevia:
 - Implantation of the placenta in the lower uterine segment near or over the internal os.
 - Graded 1 to 4 (worst)
 - Risk factors: prior c-section (uterine scar), grand multiparity (>5), multiple birth, maternal age >35, tobacco/cocaine use, fibroid uterus (ie anything that causes scarring or reduces places for embryo to attach)
 - Placental abruption:
 - Premature separation of normally implanted placenta from the uterine wall
 - Risk factors: ↑maternal age, multiparity, maternal shock, poor nutrition, gestational diabetes, ↑BP, smoking, anything that causes maternal vasoconstriction (trauma, cocaine, etc)
 - Onset of premature labour
 - Bleeding from other parts of the genital tract (eg cervical polyps, vaginitis, vulval varicosities)
 - Fetal: Vasa praevia. Bleeding from an abnormal fetal vessel attached to the membranes over the internal os. Need ROM for this to occur. Mother will not be shocked
- Clinical differences between praevia and abruption:

Placenta praevia	Placental abruption
Shock in proportion to visible blood loss	Shock out of proportion to visible blood loss (concealed)
Painless	Poorly localised abdominal pain
Bright red bleeding	Dark red bleeding and clots
No contractions, uterus well relaxed	Uterus tense and tender
Fetus easy to palpated with good heart tones	No fetal heart sound detectable
Recurrent	Possible DIC

- Assessment:
 - History: previous bleeds, initiating factors, eg trauma, colitis
 - ALWAYS ultrasound: exclude placenta praevia (detects 95 – 98% of cases) and major abruption with placental separation.
 - NO vaginal exam until praevia excluded
 - APT test to distinguish fetal from maternal blood
 - Bloods to monitor hypovolaemic shock, DIC
 - Fetal well-being, eg CTG
 - If major blood loss, treat for shock → transfuse, give O2
 - Give steroids
 - If fetus alive, consider c-section before labour
 - If fetus dead, induce
- Treatment:
 - If Rhesus negative and no antibodies yet, give Anti-D within 72 hours

- Placenta praevia: If substantial, hospitalised till delivery, Caesar at 38 weeks
- Placental abruption: Hospitalise. Serious risk of PPH, also acute renal failure, pituitary necrosis, etc. Monitor retro-placental clot by serial ultrasound

*Rhesus haemolytic disease**

- Aetiology: if Rhesus -ive mother is ‘contaminated’ by blood from a Rhesus +ive baby \Rightarrow anti-D IgG antibodies (isoimmunisation)
- Later in the pregnancy, or in a following pregnancy, IgG can cross the placenta causing Erythroblastosis Fetalis (\rightarrow stiff oedematous lungs and hydrops – widespread oedema)
- Test for anti-D antibodies in all Rhesus -ive mothers at booking and in 2nd trimester. If elevated then monitor carefully
- Anti-D immunoglobulin given prophylactically to Rh -ive mothers:
 - Within 72 hours after incident (eg amnio, threatened miscarriage, spontaneous abortion, any risk of trans-placental haemorrhage – TPH, etc)
 - After birth if baby Rh +ive or group not known
 - This prevents ‘iso-immunisation’ – gobbles up antigen before mothers immune system generates antibodies
 - Don’t give anti-D if mother already producing Anti-D

Premature labour

- = Labour < 37 weeks
- 8% of babies, 85% of neonatal deaths
- Over-diagnosed – over 80% diagnosed will deliver at term without treatment. Hard to diagnose – regular uterine contractions are normal, cervical changes in labour can be subtle
- Braxton-Hicks contractions are usual from 30 weeks but are not painful
- History: Is it true labour: check nature of contractions, urinary frequency (?UTI), backache, spotting or a change in vaginal discharge (normal in 3rd trimester – lots, white, non-smelling).
- Risks:
 - Strongest association is previous preterm birth (\uparrow 4 times risk)
 - Previous mid-trimester abortions (2 or more) – not 1st trimester spontaneous abortions
- Aetiology:
 - Spontaneous: 40%
 - Multiple pregnancy: 10%, \uparrow 10 times risk
 - Maternal or fetal conditions (25%)
 - Premature, preterm rupture of membranes (PPROM = rupture of membranes before labour commences and preterm)
 - APH
 - > 28 weeks, 80 – 90% survival
 - > 32 weeks, similar survival as term babies but complications
- Management:
 - Investigations: temperature, BP, pulse, SFH, view cervix for clots etc (do NOT view cervix if risk of praevia – do US first), ?infection screen, US, MSU, fetal welfare
 - Consider tocolysis (inhibiting labour):
 - Inhibit uterine contractions – allows time for steroids to work and for transfer to neonatal unit
 - β agonists – Ritodrine and Salbutamol (risk of pulmonary oedema) prolong labour for \sim 24 hours. Adverse effects: maternal and fetal tachycardia, vasodilation \rightarrow \downarrow BP. Contraindications: fetal distress, severe pre-eclampsia, APH, hypotension, tachycardia, asthma, etc
 - Oral Nifedipine (Ca channel blocker) is replacing Salbutamol – equal efficacy and \downarrow side effects.
 - If cervix is > 4cm then it should be allowed to progress – shouldn’t use tocolytics
 - ?Not if PROM (premature rupture of membranes). Can \rightarrow \uparrow risk of infection
 - Steroids: dexamethasone and betamethasone (crosses placenta, prednisone doesn’t) - 2 shots 12 hours apart. Always give first even if close to delivery \rightarrow maturation of lungs if between 24 and 34 weeks (\uparrow surfactant production \rightarrow \downarrow fetal distress syndrome) and neonatal better BP control post delivery
 - Delivery. If < 26 weeks then vaginal delivery. C-section more likely if multiple pregnancy or breech. Epidural analgesia preferable to narcotics (\rightarrow respiratory depression)

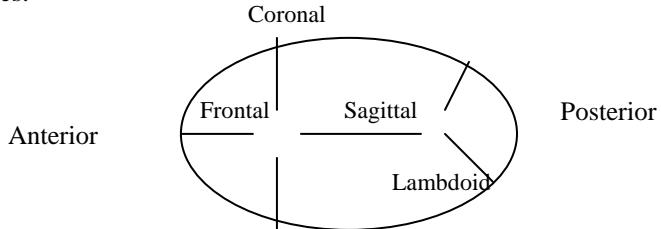
*Premature Rupture of Membranes**

- = Rupture of membranes before labour is established. Normally rupture of membranes follows establishment of labour
- Check: have they really ruptured? Look for pooled liquor in posterior fornix. Do US for liquor volume and fetal well-being
- Management:
 - Admit and monitor
 - Swabs for infection (a cause of PROM)
 - Check for signs of infection: fever, maternal or fetal tachycardia, ↑WBC
 - After 24 hours (time varies) commence prophylactic antibiotics
 - Low threshold for induction

Labour

- Definition:
 - Regular contractions (usually 3 in 10 minutes, lasting 40 – 50 seconds)
 - Cervical change:
 - More anterior
 - Effaced: depth of 'rim' normally 2 cm, 50% effaced = 1 cm
 - Dilated
 - Soft (hard = like forehead, normal = like nose, soft = like chin)
 - +/- Show (mucus plug) or ROM (rupture of membranes)
- 80% of all pregnancies last 38 - 42 weeks. 10% are preterm. 10% beyond the start of the 43rd week (although biggest cause is inability to reliably date conception)
- How does it start:
 - Uterus: ↑distension, ↑gap junctions in smooth muscle, ↑oxytocin receptors
 - Cervical ripening: PGE breaks down collagen + effect of Braxton-Hicks contractions
 - Fetus: ?vasopressin released in response to transient hypoxia, ?other hormones
- Examination:
 - Mother: monitor BP (hypo → ?blood loss, hyper → ?pre-eclampsia), pulse, temperature (eg infection if prolonged period post-rupture)
 - Foetal position: by abdominal inspection and palpation. 2/3rds of babies head first with back on the left. Descent – what portion of the head is below the pelvis (eg 3/5ths)
 - Fundal height
 - Foetal welfare:
 - CTG for 20 minutes (but incidence of fetal distress in early labour is low. Continuous monitoring → ↑interventions)
 - Intermittent auscultation every 15 – 30 minutes following a contraction. Approx every 5 minutes in 2nd stage.
- Fetal position – Definitions:
 - Lightening:
 - = Baby dropping. → ↓SFH, development of lower segment of the uterus, descent of fetal head into pelvis
 - 1st pregnancy: 2 – 3 weeks before
 - 2nd pregnancy: may not be till 2nd stage of labour – uterus has lost some of its tone – doesn't push baby down so well
 - Fetal lie: relation of fetal spine to mother's spine. Longitudinal (cephalic or breech), transverse, oblique (unstable lie)
 - Fetal presentation: portion of the fetus in the birth canal:
 - Cephalic (96%): vertex, sinceput, brow, face
 - Breech (3%): Frank (extended – 'foot in mouth'), Complete (knees and hips flexed), Incomplete (footling). Only worry after 36 weeks – it can turn fairly easily before then
 - Transverse or oblique (1%)
 - Fetal Attitude: "posture" of the fetus, eg extended neck
 - Fetal Position: Relation of occiput (vertex) to the maternal pelvis. Left or Right, Anterior, Posterior, or Transverse, eg
 - LOA = left occiput anterior (face down, 8 o'clock) – most common position
 - LOT = left occiput transverse
 - OA = occiput anterior (6 o'clock)

- LOP = left occiput posterior (face up)
- Sutures:



- Caput succedaneum: swelling of the fetal scalp immediately over the os
- Moulding: Overlapping cranial bones in cephalic presentation. May \downarrow BPD (biparietal parameter) by 0.5 – 1.0 cm
- Crowning: encirclement of largest diameter of the fetal head by the vulvar ring
- Adequate sized pelvis has:
 - Wide pubic angle (skeleton can fit a fist)
 - > 10 cm between ischial spines
 - Can't reach sacral prominence (top of sacrum) on vaginal exam
- Delivery of the baby:
 - Engagement: time when BPD passes through the pelvic inlet. Abdominal, 2/5 is palpable. If engaged, you know the pelvic inlet is big enough
 - Descent: Extension of fetal body.
 - Flexion of neck
 - Internal rotation. Head rotates from 8 o'clock to 6 o'clock. Usually descent through pelvis transverse, then need to rotate face downwards
 - Extension: once head reaches vulva, occiput in direct contact with symphysis. Ritgen Manoeuvre – upward pressure on chin through perineum from below, downward pressure on occiput (stop anterior tear)
 - External Rotation/Restitution – occiput goes back to original position (transverse) – now realigned again with shoulder. Check for nuchal cord (around neck), clear nasopharynx
 - Expulsion: anterior shoulder, followed by posterior shoulder. Clamp and cut cord, with baby below the level of the placenta if possible or if prem
 - Episiotomy: NOT routine. In NZ do them medio-lateral at time of Crowning. 1st degree = superficial, 4th degree = deep, including rectal sphincter and mucosa
- Stages of labour:
 - Stage 1: Cervical effacement and dilation - Friedman phase – plot on a partogram:
 - Latent phase (cervical softening). 20 hours in nullip, 14 hours in multip
 - Active Phase: Acceleration phase and deceleration phase (= transition). Cervix dilates 1.0 – 1.2 cm/hr (Primiparous), 1.5 cm/hour (multiparous) to a maximum of 10cm dilated
 - Stage 2: begins at 10 cm dilated and ends with delivery of the baby. 2 hours in primip, 45 minutes – 1 hour in multip.
 - Stage 3: separation and expulsion of the placenta
 - Active management of 3rd stage
 - Especially if risk of PPH (big baby/twins/previous PPH/anything that makes the uterus big eg polyhydramnios). See Postpartum haemorrhage (PPH), page 373
 - Give 5 – 10 units Syntocinon (IV if risk of PPH, IM otherwise) when shoulder delivers
 - Can use syntometrin (oxytocin + a little ergometrine – contraindicated if hypotension)
 - If PPH then IV infusion following bolus (T½ of Syntocinon is 3 – 5 minutes)
 - Complications of Syntocinon: hyperstimulation (\rightarrow \uparrow fetal hypoxia), uterine rupture, water intoxication (Syntocinon is like ADH), uterine muscle fatigue (\rightarrow post-delivery uterine atony \rightarrow \uparrow risk of PPH)
 - Signs of placental separation: sudden rush of blood, uterus rises, cord lengthens
 - OK to wait if no heavy bleeding. Gentle traction on chord with supra-pubic pressure (stops uterus coming down) or fundal massage and maternal bearing down *without* traction
 - Can manually deliver (place hand into uterus and separate) – if no haemorrhage then wait for anaesthesia
 - Then inspection, repair, rectal exam
 - Cord prolapse: Cord comes through cervix before head. C-section usually indicated. In meantime try to control pressure on cord – don't push it back up. Risk if transverse lie

- Pain Relief:
 - Inhalation agent (eg nitrous oxide)
 - Epidural: complications – hypotension, urinary retention, total spinal block, prolonged expulsive effort
 - TENS
 - Narcotics eg pethidine: action lasts 3 hours and can cause fetal respiratory distress – don't give if delivery expected within 3 hours
 - See also Obstetric Anaesthesia, page 545

Abnormal Labour

- Risks to foetus in distress:
 - Hypoxia +/- ischaemia
 - Trauma
 - Meconium aspiration (meconium = first stool. Abnormal to find it in amniotic fluid).
- = Labour does not progress normally. Due to problems with:
 - Power – eg hypoactive uterine contractions, or hyperactive (eg spasm)
 - Passage – disproportion between the size of the pelvis and the fetus (eg scarred cervix)
 - Passenger – abnormal lie, presentation, position or structure of the fetus
 - Psyche – excessively anxious or sedated mother (but if sedatives can ↓contractions then probably not true labour), conduction anaesthesia (ie epidural) may weaken lower uterine contractions and therefore not assist head rotation and flexion
- Types:
 - Protracted labour – takes longer than normal
 - Arrested labour – progresses normally then stops. During active stage, progress = *either* further dilation or further descent
 - Can happen at any stage
- Causes of failure to progress:
 - Prolonged latent phase
 - Primary dysfunctional labour: never enters active phase. Associated with primagravids, OP or deflexed neck, post maturity and unripe cervix
 - Secondary arrest: enters active phase then stops. More likely than primary dysfunctional labour to be associated with absolute cephalo-pelvic disproportion
 - Cervical dystocia: Primary (rare) or secondary (eg following cone biopsy)
- Evaluation:
 - Palpate or monitor uterine contractions
 - Perform cervical exam (and check history)
 - Determine lie/position of fetus
 - Review medication
- Treatment:
 - Hypertonic contractions – pain medication, Syntocinon
 - Hypotonic contractions – Syntocinon, AROM (artificial rupture of membranes)
- Abnormal Presentations:
 - Breech. More prone to abnormal labour. C-section if < 1000 gm (body comes through at 7 – 8 cm dilated and head gets stuck = “entrapment of after-coming head) or > 3600 or 4000 gm. C-section becoming more routine for any breech
 - Face (rather than occiput first). Occurs with complete extension. Mentum (chin) anterior can be delivered vaginally. Don't use forceps and Syntocinon
 - Brow. Incomplete flexion (midway between face and vertex). Converts to either face or occiput – can't deliver as brow
 - Occiput transverse: Head can't flex and rotate from transverse to occiput anterior. Gets stuck at iliac spines. Risk factors include pelvis shape (wide and squashed = platypoid). Rotate manually or with forceps, or C-section
 - Occiput posterior (ie face up): 5 – 10 %, prolonged second stage, painful labour (lots of back pain), bigger tears and episiotomies
- Abnormal fetal structure:
 - Macrosomia
 - Hydrocephalus
 - Hydrops Fetalis: total body oedema eg due to heart failure secondary to Rh-isoimmunisation
 - Meningocele (a neural tube defect)

- Pelvic abnormalities:
 - Inlet: failure to descend/engage (failure to descend prior to labour in a nullip is a bad sign)
 - Mid: smaller capacity than inlet, often associated with OT/OP
 - Outlet: rare in the absence of contracted mid-pelvis

Cardiotocography (CTG) in Labour

- = Fetal heart rate monitoring
- Look at rate (normal = 110 – 160), variability (> 5 bpm), accelerations (2 or more of at least 15 bpm in 20 minutes).
- Don't want: Basal rate < 110 or > 160, ↓ variability for longer than 45 – 60 minutes, or spontaneous decelerations
- Early decelerations (ie with a contraction) are probably normal (due to pressure on the head → ↓HR - ?Cushings type reflex). Late decelerations (*following* a contraction) are a sign of fetal hypoxia. "Shouldering" (brief ↑HR either side of a deceleration) may signal cord compression
- Early hypoxia is indicated by a mild tachycardia, reduced variability and consistent late decelerations. 80% sensitivity (ie 1 in 5 unnecessary interventions). A not normal but not abnormal trace has a 20 – 50% sensitivity for hypoxia
- A poor CTG is an indicator only. May do scalp sample to confirm (pH < 7.2 or base excess > -12 getting bad ⇒ deliver now by the safest means). Would act now on a bad trace if not in labour or prolonged bradycardia < 80
- Red hearings:
 - Check maternal BP. Hypotensive mother → poor trace. Eg following epidural insertion, vena cava compression (change position)
 - Hyperstimulation: contractions too long or fast → turn down syntocinon

Methods of Induction

- Prostaglandins on the cervix
- Artificial rupture of membranes
- Oxytocin drip

Forceps

- To provide traction, rotation or both to the fetal head
- Indications: delay in second stage, fetal distress, malposition, poor maternal effort, etc
- Types: outlet, mid or low – depends on the station of the fetal head and degree of rotation
- Should never be used when fetal head is not at least at 0 station (unengaged) as you don't know if the head will fit through
- Requirements: cephalic presentation, known position, contractions present (mum needs to push at same time), ROM, fully dilated otherwise cervical tear (→ ↑bleeding and possible future cervical incompetence), empty bladder and adequate anaesthesia
- Complications:
 - Maternal: vaginal, cervical or uterine laceration, bleeding, bladder or bowel injury, often episiotomy
 - Fetal: bruising, scalp, skull, eye or brain injury

Ventouse/Vacuum

- Suction applied over posterior fontanelle
- Less space necessary, often leads to spontaneous flexion/rotation, don't need to know exact fetal position, will pop off if too much pressure → less risk of trauma to mum or baby

Caesarean section

- Types (refers to uterine not skin incision):
 - Lower segment transverse: ↓risk of uterine rupture in subsequent pregnancy (<1%)
 - Classical: vertical incision in upper segment of the uterus. 5 – 6 % risk of rupture in subsequent pregnancy. ↑Bleeding, infection, ileus
 - Low vertical: vertical incision in the lower segment – treat as classical
 - Indications for classical: preterm breech, fibroids, anterior placenta praevia, transverse lie with back down
- Risks to mother:
 - 4 – 6 times greater than for vaginal delivery

- Anaesthetic risk for mother. Especially aspiration (slow digestion → usually something in the stomach). Give antacid and Maxolon (\downarrow acidity if aspirates and \downarrow vomiting). Give O2 to mum → \downarrow fetal hypoxia. Group and hold. Usually use spinal or epidural anaesthetic (although → vasodilation → \downarrow BP → \uparrow fetal distress)
- Infection
- Bleed (placenta gets 500mls of blood a minute at term). May → hysterectomy.
- DVT (pregnant, surgery and immobile) → PE (most common cause of maternal death)
- Future obstetric complications:
 - \uparrow Risk of caesarean section next time. Can normally trial labour and 70% will progress normally. 1% uterine rupture ($\uparrow\uparrow$ pain, hypotensive). Can't be induced if previous Caesar – strong contractions against a closed cervix → \uparrow risk of rupture
 - Risk of placenta growing in the scar next time. May → placenta accreta (abnormal adherence to uterus which → \uparrow risk of PPH)
- Indications:
 - Placental: praevia, abruption, vasa praevia
 - Fetal: disease (eg hydrops), malpresentation, distress, cord prolapse
 - Maternal: eclampsia, severe PET, active HSV, cardiac disease, cervical cancer, prior uterine surgery, obstruction (eg fibroids, ovarian tumours)
- Herpes Simplex Virus: Caesarean indicated if current genital outbreak at delivery. Only approx 1% of babies infected but approx 50% mortality if infected

Perinatal Asphyxia

- Asphyxia: cessation of gas exchange → hypoxia and hypercarbia. Can occur in utero, intra-partum or postnatally.
- Fetal Distress: fetus demonstrates one or more clinical indicators of hypoxia (eg early passage of meconium and HR changes on CTG)
- Hypoxic-ischaemic encephalopathy (HIE): clinical manifestation in the neonate of a previous hypoxic-ischaemic insult. Need for resuscitation (or not) at birth does not necessarily correlate with HIE later on:

Grade	Features	Mortality	Neurologic Sequelae in survivors
Mild	Irritability, poor sucking, hypotonia	0%	0%
Moderate	Convulsions, lethargy, poor feeding, abnormal tone	5%	21%
Severe	Comatose, seizures, ventilated	75%	100%

- Cerebral Palsy: See Cerebral Palsy, page 629
- Systemic effects of hypoxia:
 - Brain: hypoxic ischaemic encephalopathy (all are potentially reversible except for this one)
 - Kidney: renal failure
 - CV: hypotension
 - Liver: coagulopathy
 - Respiratory: meconium aspiration, pulmonary hypertension
 - Gut: ischaemia

Postnatal assessment

- See Examination of the Newborn, page 587

Postpartum Complications

- Maternal mortality used to be mainly due to PPH and puerperal fever, now PE is the biggest cause

Definitions of Perinatal and Maternal Mortality

- Perinatal mortality = death of a fetus after 20th week or > 500 gm through to the time of delivery + death in first week
 - Born dead = late fetal death
 - Death in first week = early neonatal death
 - Perinatal mortality rate (PMR) = (LFD + ENND)/1000 live births. In NZ is 6 – 8 per 1,000. Varies from region to region

- Reasons for perinatal death:
 - Hypoxia (eg placenta separated, maternal hypertension)
 - Prematurity
 - Congenital abnormality (eg heart defect, spina bifida)
 - Trauma (eg difficult birth)
- Maternal Death:
 - Death associated with pregnancy or trophoblastic disease up to 3 months after the event (required to be reported to Medical Officer of Health)
 - Causes:
 - Obstetric causes – 70%. Includes DVT/PE, hypertension, anaesthetic death, haemorrhage
 - Associated medical deaths (eg asthma, heart disease)
 - Associated malignancy (eg breast cancer)
 - Suicide/homicide

Postpartum haemorrhage (PPH)

- Primary PPH:
 - = Loss of > 500 ml < 24 hours after delivery
 - Limitations: estimating loss is difficult and loss may be concealed
 - Causes:
 - Uterine atony (90%). Eg in anything that causes large uterus – twins, polyhydramnios, etc
 - Genital tract trauma during delivery (7%)
 - Coagulation defect
 - Management:
 - Resuscitate mother. Test bloods for coagulopathy
 - Rub up a contraction + IV oxytocics
 - Deliver placenta and inspect for completeness
 - Inspect genital tract for trauma. Eg vaginal lacerations, ruptured uterus
 - If bleeding continues ⇒ uterine atony. IM prostaglandins + other procedures
- Secondary PPH:
 - = Loss of any volume of blood > 24 hours and < 6 weeks post delivery. Usually 1 – 2 weeks after
 - Cause: retained placenta/clot, often infected
 - Risk factors: abnormal placentation or accessory lobes on placenta
 - Diagnosis: Ultrasound +/- signs of infection: fever, tender uterus, offensive lochia (discharge after delivery)
 - Management: curettage with US guidance + antibiotics (Broad spectrum + anaerobic cover)
- Pharmacology:
 - Syntocinon: action lasts 20 – 30 minutes, causes hypotension, H₂O retention, contraindicated in CV disease (eg pre-eclampsia). Used for labour induction or augmentation
 - Ergot alkaloids (eg Ergometrine). For PPH. Causes hypertension and vomiting. Contraindicated in hypertension.
 - Prostaglandin F2α. IM for PPH. Contraindicated in Asthma, CV disease
- Sequalae:
 - Massive bleed → shock and death
 - Puerperal anaemia and morbidity
 - Sheehan's syndrome: ischaemia of anterior lobe of pituitary → pan-pituitary insufficiency
 - Fear of further pregnancies
- Prophylaxis:
 - Active management of 3rd stage
 - Elective C-section if placenta praevia
 - 50% risk next time, reduces to 20% if active management
 - If at risk, then have active management of 3rd stage labour, have wide bore cannula in place and specialist backup available

Puerperal Fever

- Puerperium
 - = Time in which reproductive organs return to their pre-pregnant state – usually 6 weeks after delivery
 - Uterus involutes from 1 kg to 100 gm. Pelvic organ by ~10 days
 - Lochia: red for day 1 – 3, yellow next 10 days, white until 6 weeks

- Puerperal Pyrexia = temperature of at least 38 C on any 2 of the first 14 days after abortion or delivery, exclusive of the first 24 hours
- Incidence:
 - After vaginal delivery: 1 – 3 %
 - After Caesarean: ~10%
- Pathogenesis: assume infection until proven otherwise. Can deteriorate quickly – need rapid assessment
- Sources:
 - Clots, retained placenta, etc can facilitate growth
 - Generally an ascending infection
 - Lower genital tract (eg anaerobes).
 - Bowel: E. Coli and G –ive
 - Attendants: staph and haemolytic strep
 - Environment or partner
- Severity is related to:
 - Bacterial factors: virulence, resistance, etc
 - Host: general health, immune status
 - Pregnancy related: duration of labour post-ROM, invasive examinations
- Causes:
 - Endometritis (uterine infection):
 - Most common cause
 - Fever, uterine tenderness on abdominal palpation, foul-smelling lochia (post-partum vaginal discharge)
 - Treat aggressively to avoid abscesses
 - Can proceed to peritonitis, septicaemia, etc
 - Mastitis: Usually occurs 2 – 3 weeks postpartum and is associated with cellulites over the affected area. Staph Aureus is common
 - UTI: ↑risk from catheterisations, operative vaginal delivery
 - Thrombophlebitis: 1% of women present with painful tender varicose veins. Look for DVT symptoms. ↑Risk if obese, high parity, bed-bound, etc. Treat with NSAID
 - Wound and episiotomy infections
 - Respiratory tract infection, atelectasis
- Investigations: FBC, urine culture, high vaginal swabs
- Management:
 - General: fluids, correct anaemia, pain relief
 - Antibiotics: start empirical treatment immediately. CCHL protocol is IV Augmentin + Metronidazole

Six Week Check

- Looking for problems that may not have been present at birth (ie don't check for imperforate anus, they'd be dead by now!)
- The main aim of the 6 week check is to:
 - Detect abnormalities in the baby that may have become clinically detectable since birth
 - Explain the advantages of immunisation for the baby and offer immunisation
 - Check the psychological and physical well-being of the mother
 - Promote breast feeding and healthy attachment
- Checks for the baby:
 - General well-being including sleeping and feeding
 - Growth: check serial measurements in the Child Development Book
 - General physical inspection, including fontanelles
 - Neurological milestones:
 - Sight (do they follow an object, smile at a face, etc): at risk if premature or birth asphyxia
 - Hearing (startles with loud noise, etc): at risk if family history, rubella, CMV, toxoplasmosis, <1500 gm, severe asphyxia
 - The mother is likely to be aware of the presence of absence of these
 - Heart: Auscultate for murmurs, look for pallor, dyspnoea with feeds, failure to thrive (1% affected, VSD in 30% of these)

- Hip dislocation: unstable hips may not present until after birth. 0.4%, girls = 5 * boys. Need to treat before they begin to walk. Investigate with US and Xray. Treat with Pavlik harness
- Genitals: Check boys for undescended testes (cryptorchidism) – 2%, especially if premature, spontaneous descent unlikely beyond 3 months, surgery at 9 – 12 months. See Undescended testis, page 636
- Checks for the mother:
 - History:
 - General well-being
 - Signs of post-natal depression or adjustment disorder: poor sleep or appetite, feeling ‘low’, anxious or guilty, thoughts of harming herself or the baby. Complete a screening survey such as the Edinburgh Postnatal Depression Questionnaire. See Postpartum Mood Disorders, page 430
 - Breastfeeding: Is this going well?
 - Bowel and urine continence – encourage pelvic floor exercises
 - Perineum: pain, dyspareunia, etc
 - Review of pregnancy and child-birth experience
 - Exam:
 - Weight: loss of 60% of weight gained during pregnancy
 - Examine breasts for infection or cracked nipples
 - Abdominal exam: involution of the uterus – should be at or approach pre-pregnant size
 - Pelvic exam: healing of laceration or episiotomy, lochia assessed, size and tenderness of uterus
 - Cervical smear if not up-to-date
 - Check of other complications that may have arisen in pregnancy: BP, diabetes, anaemia, UTIs, etc
- Contraceptive advice:
 - Low levels of sexual interest common
 - Return of fertility is variable. If not breastfeeding ovulation can occur as soon as 28 days
 - Complete breast feeding provides 98% protection for the first 6 months (provided they continue to have amenorrhoea). Normally start contraception at 3 months
 - POP: Start in early puerperium. Very effective in conjunction with breast-feeding. Start CoC when feeding frequency has ↓ by half, when solid food started or with first bleed (whichever first). Amount transferred to baby over 2 years = 1 tablet’s worth
 - COC: alters quantity and quality of milk. If not breast feeding start on day 21 (↓thrombosis risk and won’t have ovulated yet)
 - IUCD: Insert 4 - 8 weeks postpartum (higher expulsion rates if inserted after 3rd stage, and C-section scar will have healed by then)
 - Sterilisation: wait a while – may change their mind
 - Natural family planning: problematic due to variable effect of lactation on periods
- Immunisation is recommended for Diphtheria, Tetanus, Pertussis, Haemophilus Influenza type B, Hepatitis B and polio vaccine. If the mother is concerned about the baby being unsettled afterwards, prophylactic oral paracetamol can also be offered.

Breast

Physiology & Anatomy

- 3 – 4 days before menses, ↑oestrogen and progesterone → cell proliferation and water retention
- During pregnancy, cell proliferation. Post-partum, prolactin → milk production.
- At menopause, breast involution due to replacement of glandular tissue by fibrosis and fat. Occurs with age
- Superficial and deep fascia form a sandwich around the breast
- Breast is between the 2nd and 6th intercostal spaces

Breast History

- Previous lumps
- Pain
- Nipple discharge:
 - Is it blood stained

- Is it unilateral or bilateral
- Is there an associated lump
- Changes related to menstruation
- Parous state – breast feed?
- Last period
- Family History

Breast Exam

- 7 – 10 days after the beginning of menses
- Inspection: while standing, look for dimpling and nipple deformity with patient's hands on her hips and then above her head
- Palpation:
 - Patient supine with hands behind her head
 - Distinguish glandular tissue from breast fat
 - Check for loss of pliability as well as for masses
 - Axilla: checked for enlarged axillary lymph nodes – 1 – 2% of cancers present as axillary lumps
 - Characteristics of breast cancer: fixed, immobile, single, hard

Breast Investigations

- Clinician/surgeon: examination and history
- Pathologist: FNA (\rightarrow cytology) and core biopsy (\rightarrow histology)
- Radiologist: mammography and ultrasound. Clues on mammography:
 - Calcification:
 - Benign: very large, well rounded
 - Malignant: clusters, variable border, cast in a duct
 - Density

Breast in Pregnancy and Breastfeeding

- Changes during pregnancy:
 - Oestrogen, progesterone, HPL, PRL and HCG \rightarrow acinar cellular hyperplasia in early pregnancy, hypertrophy in later pregnancy, duct sprouting
 - By end of pregnancy, breast is composed almost entirely of lobules separated by relatively scant amount of stroma
- Immediately after childbirth:
 - \downarrow Progesterone \rightarrow milk production under the influence of PRL
 - Milk let down: sucking \rightarrow \uparrow pulsatile oxytocin \rightarrow myoepithelial cells squeezes milk down duct. Also due to neuroendocrine reflex (eg hearing baby cry). Sensitive to emotional stress
 - Sucking also stimulates PRL \rightarrow continued milk production
- Advantages of breast feeding:
 - Infant: \downarrow infant mortality (two fold), bonding, cheap, anti-infective properties (lysozyme, IgA, lactoferrine, etc), \downarrow SIDS
 - Maternal: contraceptive, sucking promotes uterine contractions \rightarrow \downarrow PPH, \downarrow pre-menopausal breast cancer
 - Sufficient on its own until 4 – 6 months
 - See also Breast-feeding, page 590
- Contra-indications: maternal HBsAg, CMV or HIV +ive, active breast HSV lesions, amiodarone
- Breast care:
 - Sore/cracked nipple prevention:
 - Poor position, poor hygiene, irritation (clothing, soap)
 - Treatment: shields, advice on position, break suction with finger
 - Breast engorgement:
 - Supply > demand \rightarrow enlarged breast \rightarrow baby can't latch on
 - Management: feed on demand, no other fluids for baby, express, paracetamol
 - Mastitis:
 - Cellulitis of interlobular connective tissue (mainly Staph Aureus)
 - Fever, tiredness, muscle aches and pains
 - Treatment: antibiotics (flucloxacillin), analgesics, regularly empty breast, massage lumps towards nipple when feeding

- Abscess:
 - Secondary to mastitis, febrile and toxic, red and tender > 48 hours
 - Treatment: surgical drainage, antibiotics, antipyretics, analgesics, ?suppress lactation
 - Inverted or retracted nipples: gently pull out through pregnancy

Breast discharge

- Causes:
 - Causes of galactorrhoea:
 - Physiological
 - Drug related (eg dopamine)
 - Bronchogenic cancer
 - Prolactinoma
 - Duct ectasia (periductal mastitis) – most common cause in pre-menopausal women. Discharge may be serous, greenish or bloody
 - Carcinoma: usually associated with a palpable mass – cause in 10% over age 55. Cancer unlikely if discharge is coming from both nipples and/or multiple ducts. Cytologic examination has 50% sensitivity
- Management:
 - History and exam
 - Get mammogram, re-examine in 3 and 12 months, and repeat mammogram in 12 months
 - Sample to discharge to lab
 - Check serum PRL, especially if a pre-menopausal woman has irregular periods
- Pregnancy and discharge:
 - Epithelial hyperplasia may → blood-stained discharge (usually normal)
 - Galactocoele: a milk filled cyst due to plugged duct
- Galactorrhoea:
 - Physiological: menarche/menopause
 - Secondary to dopamine: chlorpromazine, haloperidol, metoclopramide, methyldopa
 - Prolactinoma: bronchogenic cancer or pituitary tumour

Developmental Problems

- Inverted nipples are common. If a previously normal nipple inverts ⇒ cancer until proven otherwise (although nipple retraction is more likely to be inflammatory than malignant)
- Virginal/ Adolescent Hypertrophy: very large breasts developing around puberty. Problem with stroma. Aetiology unknown
- Hypomastia: almost complete failure of breast development. May be unilateral
- Accessory nipples (don't have lobular tissue underneath)

Inflammatory Breast Disease

- Acute Mastitis and breast abscess:
 - Usually occurs in early lactation
 - Usually staph aureus (abscess), less often strep (cellulitis)
- Fat Necrosis:
 - A solid mass caused by injury (eg seat belt injury)
 - Necrotic fat cells surrounded by an inflammatory infiltrate, with later calcification and scarring. Can mimic carcinoma
- Duct ectasia
 - Uncommon cause of a breast mass. Usually older woman, tender and nipple retraction
 - Pathogenesis: Dilation of larger ducts with secretions → loss of epithelium → ulceration → blood or serous discharge → infection → periductal mastitis (abscess + fibrosis) → nipple retraction
 - Histology: Chronic inflammation and fibrosis around ducts loaded with lipid and macrophage rich material
 - Cause unknown. Correlated with smoking
 - → Preductal mastitis: periareolar inflammation, abscess formation, unilateral, single duct, etc
- Plasma cell mastitis: Rare cause of a breast mass. Probably the same as duct ectasia but with ↑ plasma cells
- A tumour can block lymphatics causing inflammation ⇒ cancer is always a differential

Fibrocystic Disease

- A ‘catch-all’ category for gross and micro cysts
- Don’t call it mammary dysplasia
- Commonest disease of the breast
- Cause obscure – unopposed oestrogen a known factor. Women on combined pill get less fibrocystic disease
- Classification by size:
 - Gross cysts: very easy to diagnose on US. 40s. Drain with FNA
 - Micro cysts: usually 30’s and 40’s. May have cyclical pain. Resolves after menopause
 - Galactocoele – milk filled cyst, usually with lactation
- 5 components (either separately or together):
 - Cysts:
 - Dilated ducts containing cloudy serous fluid (sometimes bloody or infected)
 - All breasts contain microcysts during childbearing years. Abnormal when $> \sim 2\text{mm}$
 - Histology: epithelium may be flattened, cuboidal, columnar, piled up or show apocrine metaplasia. Surrounding stroma likely to be fibrous
 - Fibrosis:
 - Dense collagenisation distorting/compressing epithelial structures
 - Most common in upper outer quadrants, patient’s in 30s
 - Sclerosing adenosis:
 - Usually a tender lump in the upper outer quadrant, patient around 40
 - Benign proliferation of small ductules in a fibrous stroma, but histologically circumscribed
 - Lining cells proliferate to fill the ducts
 - Increased risk of cancer with florid (2*) and atypical (4*) hyperplasia
 - Mimics cancer both clinically and microscopically
 - **Apocrine Metaplasia:** Benign metaplastic change to tall cells with eosinophilic cytoplasm resembling those of secretory glands (eg lactation, sweat, etc)
 - Duct (and sometimes lobular) epithelial hyperplasia

Generally Benign Breast Tumours

Fibroadenoma

- Most common benign breast tumour – *no* malignant potential
- Hypertrophy of a lobule, compressed by stroma (\rightarrow sharply circumscribed), hard and very mobile – up to 2 – 3 cm diameter.
- Common in 16 – 24 years. Rapid growth for 6 months, 1/3 will regress.
- Diagnosis by FNA if < 25 years, surgical enucleation if > 35 years
- Histology: ↑fibrous tissue surrounding normal ducts that are often crushed flat. Risk of subsequent cancer = 2.17
- Cytology: cells clump together (cohesive) compared with malignancy which are normally non-cohesive
- Giant fibroadenoma: Variant:
 - Two peaks of incidence: 14 – 18 years and 40 – 50 years
 - Large: 5 – 10 cm
 - Typically oriental and black races
 - Diagnosis: FNA
 - Treatment: surgical enucleation (no excision margin)

Phyllodes Tumour

- Rare but ‘worrysome’ mixture of stromal and epithelial cells
- 30 – 50 years
- Shiny skin + vascular markings
- Wide spectrum from benign to frankly malignant. Grow rapidly
- Diagnosis: FNA + core biopsy. Cleft into the tumour on US is characteristic
- Treatment: excision with 1 cm margin
- Recur locally

Papilloma

- $< 1\text{cm}$ epithelial proliferation in a major duct just below the nipple

- Can → bloody discharge and/or nipple retraction
- 1 in 100 is a papillary carcinoma

Breast Cancer

Epidemiology

- In NZ, 1600 cases each year, 580 die. Commonest cause of cancer death in women.
- 10% life time incidence (usually over 70)
- Maori rate similar to non-Maori
- 75% diagnosed with breast cancer are over 50. Uncommon under 40. Mean age of diagnosis is 60 – 65. Younger if genetic risk
- If > 70 years, more likely to be indolent and hormone responsive. If < 35 then large and aggressive
- Survival:

	5-year survival (%)	10-year survival (%)
Stage I	80	65
Stage II	75	55
Stage III	55	40
Stage IV	10	5

Risk Factors

- Major risks:
 - Woman (100 * men)
 - Age
 - Previous breast cancer, also previous (or family) history of endometrial, prostate, or ovarian cancer
 - Biopsy showing an at risk condition e.g. atypical hyperplasia
 - Genetic predisposition (eg BRCA1 or 2 account for 5% of breast cancers)
 - Family History:
 - Most with family history don't develop it, most who get it won't have a family history
 - Risk is above population risk for only 1% of female population
 - 4% have a moderate increase in risk if:
 - A mother, sister or father developed breast cancer before 50, or in both breasts
 - More than one close relative on the same side of the family who had breast or ovarian cancer (geneticist said only genetic if 3 or more affected relatives – it is so common have to have a high incidence in family before suspecting a family loading)
- Minor risks:
 - Oestrogen exposure:
 - Slight increase for OC and Depo-Provera (only while taking it – and usually young so less of an issue)
 - Longer duration between menarche and menopause
 - First child beyond 35 or no children
 - Not having lactated → slight ↑risk of premenopausal cancer
 - Obesity
 - HRT for more than 5 years increases risk by about 30%. Risk disappears within 5 years of stopping
 - Radiation, environmental hazards
- Not risk factors:
 - Smoking
 - Small (now disproven?) relationship with low fat, high fibre diet

Symptoms

- Presenting symptoms:
 - Painless mass: 66%
 - Painful mass: 11%
 - Nipple discharge: 9%
- Usual presentation is a dominant, painless mass
- New lump or thickening
- Change in breast shape or size
- Puckering or dimpling of the skin
- Change in a nipple

- Lumpiness in one breast soon after period ends
- Pain in the breast that is unusual

Investigations

- History and clinical exam
- Mammogram:
 - Not sensitive < age 35
 - Calcifications: low risk are coarse or rounded, high risk are clustered or branching
 - Shadows: malignant are less circumscribed
- Ultrasound
- FNA → Cytology
- Core or hook wire biopsy

Pathogenesis

- Most tumours occur in the epithelial component lining the ducts and lobules. Epithelial hyperplasia (1 – 2 times risk) → Atypical hyperplasia – proliferation and atypia of ductal or lobular epithelium. Risk of subsequent cancer = 4 times.
- Tumour cells secrete cytokines → fibrosis → lump. Easier to detect in an older woman (\uparrow fat and \downarrow intra-lobular fibrosis)
- All breast cancers are different. Tumour growth rates vary considerably. On average takes 9 years to reach 1 cm.
- Death is from metastases which can occur at any time
- Spreads to lymph nodes via lymphatics *and* directly to distant sites via blood stream – not via lymph nodes then to distant sites (although lymph node involved \Rightarrow \uparrow risk of blood spread as well)
- Lots of implicated genes. Those in familial breast cancer include:
 - BRCA1:
 - Autosomal dominant (but recessive at the level of the cell): if carrier then 65 – 75% risk (ie high penetrance)
 - A tumour suppressor gene, expressed in breast, ovary, thymus, testis
 - Accounts for 40 – 50% of familial breast cancer
 - BRCA2:
 - Associated with male breast cancer, not ovarian
 - 10% of inherited breast cancer

Classification of Breast Cancer

- Classification:

	In-situ	Infiltrative (invasive)
Ductal	Intraductal carcinoma	Infiltrating ductal carcinoma: <ul style="list-style-type: none"> • No special type (NOS) • Medullary carcinoma • Mucinous carcinoma • Tubular carcinoma • Metaplastic
Lobular	Non-infiltrating (in situ) lobular carcinoma	Infiltrating lobular carcinoma

- Most cancers are intraductal
 - Plus Paget's Disease of the Nipple
- **Non-infiltrating/in-situ breast cancer:** Does not metastasise but recurrence is a problem. Can become infiltrative and then metastasise
 - Intraductal carcinoma (20 – 30%):
 - Comedocarcinoma: solid intraductal proliferation, central necrosis, microcalcifications on mammogram
 - Classified by nuclear grade (low, intermediate and high) and the presence or absence of necrosis.
 - Can eventually become invasive: removal → cure
 - Paget's disease (a type of ductal carcinoma in situ): lesion of the nipple caused by malignant cells arising from ducts and invading the nipple epithelium. Looks inflamed (early on can look like eczema). Most often an underlying duct carcinoma.
 - Lobular carcinoma in situ:

- Usually an incidental finding on biopsy affecting terminal ductules
- Proliferation of terminal ductules and acini
- 1% per year risk of invasive carcinoma in same *or* opposite breast – removal isn't necessarily cure
- **Invasive/infiltrating breast cancer:**
 - Main risk factor: ↑age
 - Infiltrative ductal carcinoma (65 – 80%):
 - No special type: Most common. Grossly stellate or multinodular and very hard. Histologically compressed ductules in a very desmoplastic stroma
 - Medullary: Big, bulky and soft, plentiful lymphocytes, better prognosis than other types
 - Mucinous (colloid, gelatinous) carcinoma: Grossly: gelatinous mass. Histologically: clumps of cells in lakes of mucin. Better prognosis
 - Tubular Carcinoma: well-formed glands, best prognosis
 - Infiltrative lobular carcinoma:
 - Histological: Indian files around ducts, small cells
 - Often bilateral
- Features of invasive cancers:
 - Usually dominant mass
 - Usually painless
 - In time fixed to deep fascia → immobile
 - Orange peel appearance: blocked lymphatics → oedema + suspensory ligaments contract → distorted shape
 - Also nipple retraction, ulceration of overlying skin
 - Majority arise in the outer quadrants – particularly the upper, outer quadrant
- On mammography:
 - Infiltrative edge: not well demarcated
 - ↑Density compared with adipose tissue
 - Micro-calcifications: small clustered areas of necrosis

Prognosis

- Stage: axillary metastases most important, also size. Cancers found on mammography or by self-examination are smaller ⇒ better prognosis
- Grade
- Oestrogen receptor sensitivity: if positive then better – more differentiated and Tamoxifen → regression

Treatment of Breast Cancer

- Can't cure metastases → aim of treatment is local control
- Options:
 - Two options (similar long-term survival):
 - Removal of the lump + radiation therapy (significant ↓ in local recurrence)
 - Mastectomy (or radical mastectomy) + reconstruction
 - +/- Radiotherapy (planned to limit dose to the heart, lung or opposite breast)
 - +/- Tamoxifen (anti-oestrogen)
- Surgery:

Mastectomy	Breast Conservative
Patient preference	Patient preference
Large tumour or Large tumour/breast ratio	Small tumour or small tumour/breast ratio
Multiple tumours	Single tumour
+ive margins	Focal microcalcification
Previous breast RT	-ive margins
Pregnancy, etc, etc	

- Most common metastasis is in the bone. Bisphosphonates → slow osteolysis
- Risk factors for recurrence in breast cancer (⇒ consider adjuvant chemo):
 - Axillary node status (strongest predictor)
 - Tumour size (> 1 cm)
 - Histological tumour type and grade
- Adjuvant Chemotherapy:

- Approx 25 – 30% ↓ risk of recurrence, 15 – 20% ↓ risk of death. Improves long term survival in node positive and node negative disease
- 4 to 6 courses over 3 – 6 months optimal
- 2 agents better than one: eg
 - AC: Adriamycin (an anthracycline) and Cyclophosphamide. ‘Gold standard’. Adriamycin causes vomiting and wasn’t used so much until 5HT3 antagonists were available
 - CMF: Cyclophosphamide, Methotrexate and Fluorouracil (another ‘Gold Standard’)
- Hormone Therapy:
 - Aim: prevent breast cancer cells from receiving stimulation from oestrogen
 - Only is oestrogen receptor sensitive
 - Oestrogen deprivation:
 - Block oestrogen receptor: eg Tamoxifen – antagonist. Taken for 5 years. Side-effects:
 - Largely well tolerated
 - 1 in 3 have post menopausal flushes, vaginal dryness/discharge
 - Initial nausea, weight gain
 - Rare retinopathy
 - Agonist in the uterus → ↑endometrium → ↑risk of endometrial carcinoma (1 in 1000, usually curable)
 - PE/DVT (1 – 2 %)
 - Suppress synthesis: aromatase inhibitors (work in adipose tissue, eg in post menopausal women), LHRH agonist (pre-menopausal, switches off the ovary)
 - Destroy ovaries (surgery or RT)
 - Leads to ↓recurrent, ↓ 40% incidence of contralateral breast cancer (although absolute risk low)

Breast Screening

- Of proven benefit in reducing mortality in women over 50: benefits under 50 unclear
- 2 yearly screening after 50 reduces chances of dying from breast cancer by about 1/3. Reduces a one in 42 chance to one in 60
- In NZ is free from 50 – 64
- Mammograms less reliable in under 50s: denser breast tissue. Higher false positives → ↑unnecessary investigations. Sensitivity for < 50 years is 50% - 60%, for > 50 years is 80+%. 5 – 10 % screened sent for further investigations. Positive predicative yield is 8.5% (high false positive rate)
- Further investigations: ultrasound, FNA, biopsy
- Of 1000 screened, 70 to 120 will be positive, 10 to 30 will proceed as far as open biopsy, and 5 to 10 will have cancer
- Mammogram less accurate if on HRT
- Interval cancers: fast growing cancers appearing between mammograms – never ignore a lump
- Application of screening criteria (see Criteria for Screening Programmes, page 690):
 - It is an important health problem – with a significant incidence. It is preventable
 - A screening test is available: a two yearly double view double read mammography (double reading increases cancer detection by 15% compared with single reading and reduces recall rate)
 - The screening test is available, acceptable (83% a little uncomfortable only), reasonable sensitivity, but low PPV
 - Natural history is well understood, and there is a detectable pre-symptomatic stage
 - Screening leads to interventions that increase the quality of life: relative risk reduction 10 – 30% for women in the 50 – 65 age group. However, lots of unnecessary interventions, and for a majority (>70%) whose cancer is diagnosed, the outcome is unchanged (but will live with 2 years extra knowledge of condition)
 - Is there an appropriate infrastructure to provide screening and follow-up? There have been pilot studies
 - Is it cost effective: Needs at least 70% screening coverage to be cost effective.

Sexual Health

- References: Wellington Sexual Health Service, 4th and 5th year Handout, 2000

Sexual History Taking

- Purpose of sexual history is to determine:
 - Whether or not there has been a risk of exposure to an STI including HIV

- If it is an appropriate time to take tests (window period – genital tests are not taken unless at least 14 days has elapsed from unprotected sex, unless symptomatic. For blood tests wait 3 months)
- Who else had been at risk and may need testing/treating
- Approach:
 - ‘Going to ask personal questions – want to be able to offer right tests and care’
 - Ask why they’ve come
 - Use patient’s language
 - Don’t make assumptions about anyone
 - Lot’s of reassurance: STD’s are common, confidentiality, support relationship issues – let them decide, continue at a later date
 - Not interested in their orientation but what they do
- Questions:
 - Are you sexually active?
 - How many partners have you had in the last 6 months – male or female?
 - Alcohol and drug history
 - Do you suspect that you may be at risk from HIV or other STD?
 - Need to ask about sexual abuse – won’t volunteer it: Ever had sex when you didn’t want to, ever been sexually assaulted?

Exam

Female

- Inspection: pubic lice, genital warts, ulcers, blisters, scabies
- Palpation: inguinal lymph nodes
- Vaginal examination with speculum
- Bimanual examination of pelvis

Male

- Examination of external genitalia
- Palpation of inguinal nodes
- Palpation of scrotal sac and testes

Sexually Transmitted Diseases (STDs)

- Types and incubation:
 - Chlamydia (7 – 21 days) ⇒ don’t test till 14 days after contact (unless symptomatic)
 - Gonorrhoea (range 1 – 14 days, commonly 2 – 5 days)
 - Trichomonas (3 – 21 days)
 - Herpes Simplex Virus (2 days onwards – maybe years)
 - Human Papilloma Virus (2 – 4 months, up to a year, vertical transmission possible)
 - Human Immunodeficiency Virus (HIV) – (seroconversion illness 2 – 6 weeks after exposure, HIV antibodies almost always present after 3 months. Mean time to developing AIDS defining illness 9 – 12 years)
 - Hepatitis B (1 – 6 months)
 - Syphilis (9 – 90 days)
 - Non-specific urethritis
 - Pubic Lice (eggs – 2 weeks to mature, larvae – 1 week to mature)
 - Scabies (3 – 30 days, 6 weeks for itch to develop)
 - Hepatitis C and A may be sexually transmitted
- Not necessarily sexually transmitted:
 - Normal anatomical variants
 - Commensals → bacterial vaginosis
 - Dermatoses
 - Candidacies (commensals)
 - Molluscum contagiosum (3 weeks – months)
 - Urinary tract infections
 - Prostatitis
 - Vulval disorders

Tests for STD's

- Urethral swab or first pass urine for chlamydia
- Anal or throat swab for gonorrhoea if appropriate
- Female:
 - Cervical sample for gonorrhoea, chlamydia (endocervical cells needed)
 - Cervical smear
 - High vaginal swab for bacterial vaginosis, candida, trichomonas
- Male: Urethral swab for gonorrhoea
- Blood tests:
 - Hepatitis B (Ag and Ab) and C (Ab)
 - Syphilis: VDRL, TPHA
 - HIV Ab if appropriate with counselling and consent. Always attend for results

Vaginal Discharge

- Cervical secretions in women not on the pill, and which change during the cycle, are part of normal discharge. Mucus is clear or clear/white. Some inflammatory cells are normal in the latter half of a cycle
- Desquamating vaginal cells with healthy lactobacilli are major part of normal discharge – pH < 4.5
- Key history questions:
 - Colour
 - Odour
 - Itch
- Differential:
 - Thrush (Candidiasis): white curds, very itchy, not smelly
 - Trichomoniasis: grey/green discharge, fishy smell, moderate itch
 - Bacterial Vaginosis: green, fishy, itchy
 - Chlamydia: asymptomatic or discharge
 - Atrophic vaginitis: brown, spotty discharge (from bruising), pain, no itch. Treatment: oestrogen cream or HRT

	Bacterial Vaginosis	Trichomoniasis	Candidiasis
Prominent symptoms	Discharge odour	Discharge, vulval irritation	Itch
Classical signs	No vulvitis or vaginitis	Vulvitis, vaginitis, strawberry cervix	Vulvitis, vaginitis – fissured and sore
Classical discharge	Greyish-white, thin, may be frothy	Green/yellow, watery, pools in posterior fornix, may be frothy	White, flocculent, thrush plaques
Risk factors			
Vaginal pH	pH > 4.5 (often 5.0 – 6.0)	pH > 4.5 (often 6.0 – 7.0)	pH < 4.5 (often 3.0)
KOH test (amine/Whiff test)	Positive	Weakly positive	Negative
Wet mount preparation	Clue cells present (vaginal cells covered by anaerobes & Gardnerella vaginalis). Replacement of lactobacilli with small coccobacilli (Gardnerella) or motile curved rods (Mobilunus). Few pus cells	Trichomonads (motile flagellate), pus cells	Yeast cells (blastospores)
Gram stained smear	Clue cells: G-ive curved rods. G variable coccobacilli.	Pus cells: acridine orange stain	

Notes	Also called Gardnerella. Multiplication of anaerobic bacteria and gardnerella. Associated drop in lactobacilli ↑Risk of prem delivery	Possibly commonest STI worldwide – mainly 3 rd world. A Protozoa. Doesn't culture well. Can cause PID, prem delivery. Exclude gonorrhoea	Most common cause of discharge Candida albicans often normally present. Poor immunological control → recurrent candidiasis
Treatment	Anti-anaerobe: oral metronidazole	Oral: doxycycline (remember 7 day rule)	Clotrimazole pessary

Neisseria Gonorrhoeae

- Description: G -ive diplococci
- Symptoms:
 - Male: 80% symptomatic. Discharge & dysuria (razor blade pain). 30% also have chlamydia
 - Female: only 20% symptomatic – can have vaginal discharge or pelvic pain. Pick up with opportunistic/selective screening if under 25, multiple partners, changed partner in last 6 months, IUCD, etc
 - Rectal and pharyngeal: often asymptomatic
- Diagnosis: gram stain microscopy if symptomatic or contact, or culture on chocolate agar
- Advice: no sex until minimum of 3 days since treatment completed
- Treatment:
 - Amoxycillin 3 gm and Probenecid 1 gm stat (not longer standard due to ↑ penicillin resistant), or
 - Ciprofloxacin 500 mgs (a quinolone) stat if penicillin allergy or if resistant. Specialist endorsement required. If resistant to that then Ceftriaxone (common in Auckland).
 - Azithromycin will cover gonorrhoea if it is being used to treat concurrent chlamydia
 - Resistance possible
- Contact tracing required. Treat partners
- Test for cure at 14 days (legal requirement)
- Complications: See Pelvic Inflammatory Disease (PID), page 386

Chlamydia Trachomatis

- Description: obligate intracellular bacteria, STIs are types D – K. Highest in 20 – 24 year age group
- Symptoms:
 - Urethritis, unexplained cystitis, mucopurulent cervicitis, pelvic pain, irregular bleeding
 - 80% of females and 50% of males have no symptoms. Suspect and test if sexual contacts have it, if patients asks for STI tests, patients under 25 with new/multiple partners
 - Up to 30% associated with concurrent N Gonorrhoea infection
- Diagnosis:
 - Female: swab from affected area, including from endocervix. Rotate 6 – 10 times. Urine test alone not sufficient. Most common site of single infection is cervix (ie urine is clear)
 - Male: urine test
 - New PCR test easier sampling (urine test)
 - Opportunistic detection has been shown to reduce rates of PID and ectopic pregnancy
- Advice:
 - Abstain until treated – if not use condoms
 - Contact trace
- Treatment:
 - Without test results: Doxycycline 100mgs bd for 7 days (remember 7 day rule for patients on OC)
 - Known positive **and** partners: Azithromycin 1 g stat orally – directly observed treatment
 - In pregnancy: erythromycin ethylsuccinate 800mg qid for 7 days – must be treated to prevent amnionitis and premature rupture of membranes
 - In PID: Doxycycline/erythromycin for 14 days and ornidazole 500 mgs bd for 7 days, plus consider gonorrhoea in which case penicillin/ciprofloxacin in addition
 - Test of cure in 3 weeks if non-compliance or re-infection suspected. Urine test is adequate for males and females
 - Test high risk patients only for cure
 - If reinfection, then ?untreated partner

- Complications:
 - Neonatal: conjunctivitis, pneumonitis 2 – 4 weeks later
 - See Pelvic Inflammatory Disease (PID), page 386

Herpes Simplex Virus (Type 2)

- See Herpes Simplex Virus (HSV), page 503

Pelvic Inflammatory Disease (PID)

- ~ Tubulo-peritoneal Disease
- Cause: ascending infection of vagina and cervix to endometrium, fallopian tubes and other structures:
 - Chlamydia – often chronic
 - Gonorrhoea – often acute
 - Can also be anaerobes (e.g. after instrumentation of the uterus or long standing PID)
- Symptoms: Acute pain, but 30% asymptomatic, dyspareunia (pain on sex)
- Risk factors:
 - Young age (< 25)
 - ↑Sexual activity, multiple partners, multiple infections
 - Postpartum infections
 - IUCDs in first several weeks after insertion
 - Decreased rates with condoms, diaphragms, spermicides (bacteria can use sperm as vector), tubal ligation, OC pill
- Diagnosis:
 - Difficult to make clinically: there are multiple causes of abdominal pain
 - Cervical motion tenderness (also occurs with ectopic pregnancy)
 - Purulent cervical/vaginal discharge
 - Oral temperature > 38 C
 - Irregular bleeding and break through bleeding on the OC pill
 - Ultrasound of no help. Test for other STIs. May require laparoscopy
- Treatment: Antibiotics must cover anaerobes, chlamydia and gonorrhoea. E.g. Doxycycline 100 mg bd for 10 – 14 days plus an anti-anaerobe such as metronidazole or ornidazole
- Sequelae:
 - Often repeat episodes due to:
 - Continued at risk behaviour
 - Partner is not treated
 - Past infection compromises cilia of the fallopian tubes making another infection more likely
 - Infertility risk after 1 infection is 11%, but up to 54% after 3 infections
 - Other sequelae: ectopic pregnancy, adhesions, chronic pelvic pain

*Reiter's Syndrome**

- Triad of arthritis (big joints – hot, red swollen, bilateral), urethritis and conjunctivitis
- 10:1 are males, usually 25 – 35 years
- Often (not always) caused by chlamydia (an immunological reaction, HLA B27+ more susceptible)
- Treatment: treat residual infection, if any
- See Reiter's Syndrome, page 276

Genital Warts

- Can get anal warts without anal intercourse
- External warts usually benign (types 6 & 11 – not oncogenic)
- Treatment:
 - Destructive: Condyline, liquid nitrogen – high recurrence rate
 - Imiquimod – topical cream, up-regulates immune system, expensive (\$150 per month), 19% recurrence, requires treatment for 8 – 12 weeks
- A vaccine is at stage 3 trials

Non-Sexually Transmitted Genital Skin Lesions

- Not all skin lesions on the genitals and surrounding areas are due to STDs
- Normal anatomical variants:
 - Pearly penile papules: small papillae around the corona of the penis
 - Sebaceous cysts of the penis, labia minora and scrotum

- Normal papillae in the vaginal vestibule: can be mistaken for warts
- Dermatoses:
 - Contact dermatitis: soaps, deodorants, etc
 - Psoriasis: especially head and corona of the penis. Red, scaly plaques. Not itchy. Look for it elsewhere
 - Reiter's Syndrome: urethritis, conjunctivitis, arthritis in addition to skin lesion
 - Lichen Planus: itchy plaques on the penis
- Infections (not necessarily sexually acquired):
 - Seborrhoeic dermatitis: a fungus, red, sharply defined area covered with honey coloured scales
 - Candidiasis: red, irritating, itchy rash. Treat with Clotrimazole (Canesten)
 - Dermatophyte infections (tinea) are common. Characteristic spreading edge, itchy
 - Folliculitis: small pustule around a hair follicle
 - Scabies: red, itchy nodules – may not resolve despite treatment. Treat with malathion 0.5%
 - Erythrasma: scaly, flat, brown, pigmented rash, not itchy. Caused by corynebacterium
 - Molluscum contagiosum: may be sexually acquired. Small, pearly umbilicated lesions on the thigh and buttocks

HIV

- See AIDS, page 308

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4th and 5th Year Medicine Study Notes

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Did You have to make it quite so complicated?*

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Mental Health In New Zealand

Epidemiology

- Prevalence
 - Severe mental illness: 3%
 - Chronic and/or disabling: 5%
 - Mild and/or transient: 19%
 - No mental health problems: 73% - includes up to 25% who don't meet diagnostic criteria, but face disability in function. Source: Wilson 1997
- NZ Spending:
 - Mental illness: 8%
 - All other Illness: 92%
- Youth Problems in NZ
 - 17% have had a major depressive episode
 - 10% alcohol dependence
 - 11% social phobias
 - 3% attempted suicide
- Disorders commonly presenting in primary care:
 - Depressed mood
 - Anxiety
 - Unexplained physical symptoms
 - Cognitive disturbance
 - Substance Abuse
 - Sleep disturbance
 - Sexual dysfunction
 - Weight change or abnormal eating
 - Psychotic symptoms
- International (World Bank) – Disability Life Years Lost
 - Mental Illness: 17%
 - All other illness: 83%
- Christchurch psychiatric epidemiology study, adults from 18 – 64:

	Total Population	Male	Female
Affective Disorders	9.4%	6.3%	12.4
Substance Abuse	9.1%	15.4%	3.0%
Schizophrenia	0.2 (underestimates)		
Anxiety	8.4%	5%	12%

- Key criteria for all illness is impairment of function

Maori Mental Health

- Reference: Trends in Maori Mental Health 1984 - 1993, Ministry of Maori Development
- Maori admission rates compared with Pakeha: females similar, Maori males 2 times pakeha
- Maori readmission rates have grown faster than non-Maori. Maori males 2 times more likely to be readmitted
- By specific diagnoses:
 - Maori drug and alcohol first admission rates rising relative to non-Maori
 - Maori admission rates for schizophrenia are similar to pakeha, readmission rates are higher
- Maori more likely to be referred to mental health services by welfare or law agencies than by a doctor (opposite for Pakeha)
- Maori more likely to be compulsorily admitted
- Issues:
 - Maori view of mental health and illness vs. Western psychiatric paradigm
 - Specifically Maori services
 - Maori workforce development
- Issues in treating a Maori patient:
 - Uncertain identity and alienation from society → distrust of practitioner
 - Must use interventions that enhance a Maori sense of well-being. Whanau must be basic unit of service delivery. Therapeutic alliance is with whole family, not just patient

- Complexity of problems → lots of agencies involved in care (eg illness, substance use, poverty)

Mental Health System

- Influences over the last 20 years:
 - Individualised care
 - Community based delivery: psych hospitals were very expensive and only cared for small proportion of people with mental illness
 - Consumer empowerment and patient rights
 - General management (during 80's – non-clinical people involved in management)
 - Purchaser-provider split
 - Competition
 - Public reactivity
 - Thinking about disability as well as illness

Aetiology of Psychiatric Disorders

- *Predisposing factors:* Determine a person's vulnerability to psychological distress. Causes include:
 - Genetic endowment (eg strong genetic component in psychosis)
 - Environment in utero → minor damage to CNS
 - Personality: combination of genetic, uterine development, childhood experiences (physical, psychological, social), adolescence. Particular personalities are prone to certain disorders. Eg early obsessional traits may → obsessive-compulsive disorders
- *Precipitating Factors:* Factors that occur shortly before the onset of the disorders and are likely to have caused it. Eg:
 - Physical: hypothyroidism, drugs, drugs of abuse, head injury (either direct disturbance or due to associated stress)
 - Psychological: eg loss of self-esteem owing to relationship or financial catastrophe
 - Social: eg moving house, changing job, family disturbance
- *Perpetuating factors:* Factors that prolong the course of the disorder: eg secondary demoralisation
- Psychiatric aspects of physical illness:
 - Most common psychiatric illnesses in physical illness are mood disorders and acute organic mental disorders
 - Occurs in one of three ways:
 - Psychological distress can precipitate mental illness
 - Physical distress can cause psychological ill-health (as can the medicines for physical disease)
 - Physical and psychological disorders may exist simultaneously and independently (especially in the elderly)
 - Pain: a common medical symptom. Can cause (eg head, neck, lower back, abdomen, genitalia) or arise from psychological disturbance (eg facial pain – antidepressant therapy can be effective).

Psychiatric History

Summary

- Reasons for referral
- Presenting symptoms and duration
- History of Current Illness, any medication and compliance with it
- Systematic enquiry: anxiety, mood, psychotic symptoms, suicidality, cognitive, neuro-physiological, alcohol and drug, stressors, medications, impulse-control screen
- Past psychiatric history
- Medical History
- Family History
- Personal history
- Premorbid personality
- Patient's attribution of illness
- Mental State: appearance and behaviour, speech, mood, affect, thought form, thought content, suicidal ideation, perceptual phenomena, cognition, intelligence, insight and judgement, rapport
- Formulation
- Diagnosis and Differential Diagnosis

- Management Plan
- Suicide Assessment:
 - Trying to assess nature of suicidal ideation and state of current plans
 - Predisposing factors: family history of suicide, psych illness, or alcohol & drug, personality, childhood and developmental difficulties, suicide exposure, other illness, environment (eg living alone, isolated), age and sex
 - Precipitating factors (short-term risk factors): major/stressful life event, current mood, thoughts about the future, mental state (eg psychosis, judgement, impulsivity), alcohol and drug use, current plans, expectations of outcome, availability and lethality of method
 - Protective factors: cognitive flexibility, strong social supports, hopefulness, treatment of disorders, responsibility for children
- For screening for psychiatric illness in teenagers see HEADSS Risk Assessment, page 666

History

- This will include the patient's narrative, and is therefore subject to revision and embellishment according to the state of mind of the individual and the relationship with the interviewer. The patient may adjust the history according to the interviewer's hypothesis and values. History taking is therefore collaborative and therapeutic. It is helping to construct the illness story
- **Identifying Data**
 - Name, date of interview, age, sex, race, country of birth, occupation, date of hospital admission, marital status
 - Use as opportunity to put the patient at ease, build rapport
- **Reasons for and circumstances of referral/admission**
 - Who made the referral, why now, what expectations
- **List of presenting symptoms and their duration**
 - List each symptom and duration, use patient's own words
 - Is the situation acute or chronic
 - Suggested questions:
 - What sort of problems are troubling you/were troubling you when you came to hospital?
 - What have been the main difficulties
- **History of Current Illness**
 - Need to know the patient's story: patient's situation and preceding/precipitating events
 - Narrative account of development of symptoms
 - Include medication and compliance
 - Suggested questions:
 - When did you last feel well?
 - What are the worst worries in your life?
- **Systematic enquiry**
 - Should screen for all these in every patient
 - **Anxiety** Symptoms
 - See History Taking in Anxiety Disorders, page 422
 - **Mood** Symptoms
 - Refers to long-term/sustained emotional state (ie over last week/months) and is subjective experience of the patient
 - Prevailing mood at the time: quality (eg depressed, sad, angry, irritable, happy, elated, suspicious, perplexed, anhedonia), intensity (ask about extremes), reactivity, duration (when was it last normal)
 - Persisting or fluctuating: if so what pattern
 - Aggravating or relieving factors
 - Associated symptoms
 - Patient's attribution of mood
 - **Psychotic** symptoms
 - = Thought disorder, delusions or hallucinations
 - Thought disorder = abnormalities in the thinking process – evidenced by disorganized speech, thinking or behaviour
 - Delusions
 - = Fixed, false belief, abnormal/bizarre beliefs held with conviction, are without evidence and are culturally inconsistent
 - Fixedness is key, resisting coercion to change, and preoccupying

- Ask about unusual concerns, preoccupations, thoughts that others find strange
 - Hallucinations = abnormal perceptual phenomena. Ask about visions, sensations, noises that are unusual or not shared by other people
- **Suicidability** or other dangerous behaviour: See Suicide Assessment and Management, page 416
- Cognitive functioning: See **Cognition**, page 416
- Neurophysiological changes
 - Measure severity of primary process
 - Changed sleep, energy/motivation, concentration, appetite/weight (look for a 5% change over several weeks), sex
 - Sleep: initial, middle, terminal phases, how much in total, is it restful
- Alcohol or drug use
 - Present or past
 - Smoking, alcohol, illicit drugs, sleeping tablets/tranquillisers
- Stressors
- Medications and Compliance
- **Impulse-Control** Screen: Screen for gambling (comorbidity of gambling with other psych symptoms is common)
- **Past Psychiatric History**
 - Dates, duration, diagnoses, treatment, response to treatment and outcome
 - Suggested questions:
 - Have you had any psychiatric treatment before?
 - Is the present illness like the previous one?
- **Medical History:** Past serious illnesses, disabilities, current illnesses and medication
- **Family History**
 - Parents and siblings: age, state of health (mental & physical), occupations, situation, personalities, relationship to patient. May help to draw up a family tree
 - Get idea of family atmosphere during childhood: personalities of parents and relationships have lasting influence on subsequent relationships. How much care did you get from each parent? How controlling/protective were they?
 - Ask about grandparents, and parents up bringin
 - Has anyone in the family been treated for nerves, had a breakdown, been admitted to a psych hospital, committed or attempted suicide, had an A & D problem?
 - Categorise under:
 - Structure of family
 - Description of key people
 - Description of important relationships
 - Family roles
 - Family history of psychiatric illness or alcohol abuse
- **Personal and Social History**
 - Important events and influences in patient's life
 - Start open ended: Tell me a bit about your childhood and background? What are the important things you remember?
 - Birth: difficulties, parents situation at time
 - Childhood: family situation, illnesses, injury, nervous symptoms (eg enuresis/bedwetting, fears, phobias, how did they feel going to school, etc). Did you ever have any unpleasant experiences – did anyone ever harm you, hit you, interfere with you sexually?
 - School: primary to tertiary. Academic, sporting, relationships with peers and teachers
 - Employment: types of jobs, reason for leaving, work performance & satisfaction, relationships at work
 - Sexual: age at puberty, sexual orientation, sexual experience (current and past), sexual satisfaction, contraception, sexual abuse, unpleasant or distressing sexual experiences. Introduce when talking about adolescence. Aim is to establish abnormalities or concerns about sexual functioning or relationships
 - Marital: duration of courtship, age at marriage, age, occupation and health of spouse, marital relationship and problems
 - Children: pregnancies, ages and names of children, health, personalities, schooling, occupations, difficulties in relationship with parent
 - Friendships: long-standing friends and confidences
 - Current living situation

- Difficulties with law
- Leisure activities and interests
- Religion: upbringing, beliefs and practices, changes in religious belief (important to ask, won't volunteer)
- **Premorbid personality**
 - Patient's opinions and interviewer's impressions of premorbid personality
 - Personality = enduring characteristics, so requires evaluation over time
- **Patient's Attribution of Illness**
 - What the patient thinks is the cause of the illness
 - Possibility include under 'insight' in mental state exam
- Insert **Mental State Exam** write-up here (See Mental State Examination, page 414)
- **Formulation**
 - Core of the psychiatric assessment: why did this person become ill in this way at this time?
 - Opinion about what explains the presentation and what treatment may work
 - Manner in which patient's problems are unique. Not a summary of problems but the crucial factors, based on a theoretical knowledge of the aetiology of psychiatric illness. The linkages/connections between different aspects should add something new – all the raw material should have been presented before
 - Should cover the 4 Ps: Predisposing factors, precipitating factors, perpetuating factors, protective factors
 - Conceptualise by filling in this table:

	Predisposing	Precipitating	Perpetuating	Protective
Biological				
Psychological				
Psychosocial				
 - Suggest outline (one paragraph per bullet):
 - Describe problem
 - Why is this patient at risk of a psychiatric illness, using bio-psycho-social framework
 - Describe triggers to presentation
 - Describe relevant prognostic factors, positive and negative
 - Balanced assessment of risks: especially of suicide and violent behaviour
- **Diagnosis and Differential Diagnosis**
 - Manner in which patient's problems are similar to others (cf formulation which emphasises uniqueness)
 - Usually presented using DSM-IV or ICD-10. (See DSM IV Classification*, page 418)
 - In differential diagnosis: concisely state evidence for and against each possible diagnosis in order of probability – only include evidence that discriminates between diagnoses
 - Don't forget general medical conditions if there is sufficient evidence
- **Management Plan**
 - Safety: how will the risks identified be contained or minimised. Is the patient consenting or committed?
 - Medical: any medical conditions requiring attention
 - Diagnosis: is it clear? If not, what needs to be done?
 - Psychiatric Management: can be divided into management of target symptoms and management aimed at underlying disease. Can be considered under bio-psycho-social headings. Divide into timeframes – now, the next day or two, longer term
 - Always mention family in plan: information and support for them, their role in helping the patient, assistance with the significant stresses the family may face, etc
- **Experience Interviewing the Patient:** difficulties interviewing the patient, reactions/emotions evoked by patient, how you dealt with these

Mental State Examination

- This is NOT an assessment of cognitive function (the mini-mental state is about cognitive function, but is just part of a description of mental state)
- **Appearance and Behaviour**
 - General appearance: physique, hair, make-up, tattoos, scars, clothing (self neglect, incongruous dress, weight loss)
 - Facial expression: suggestion of depression, anxiety, physical disorder (eg parkinsonian syndrome)
 - Posture

- Movements: mood and involuntary movements (tics, dystonia, akathisia, tardive dyskinesia, parkinsonism), psychomotor agitation (eg how long to answer a question)
- Social behaviour: over familiar, disinhibited, withdrawn, preoccupied, co-operative or not, bizarre behaviour
- **Speech**
 - Rate – fast/slow, Quantity – a lot/little, Loudness – loud/soft
 - Spontaneity, Continuity, Articulation, Prosody, Pressure
- **Mood:** Prevailing mood at the time. The patient's subjective experience, what they report. Note fluctuations (eg diurnal variation in depression is common)
- **Affect**
 - Refers to the objective appearance of emotions observed during the interview: anger, anxiety, elation, irritability, depressed, etc
 - Quality, intensity, stability, range
 - Variations: labile, restricted, blunted, flattened, inappropriate, fluctuating
 - Appropriateness: congruous with thinking or not
- **Thought Form**
 - May be best demonstrated by direct quote
 - Is there a logical connection between ideas or not – from an opening statement through to a goal
 - Then define type, eg:
 - Loosened associations
 - Flight of ideas
 - Derailment
 - Thought block (just stops)
 - Tangential (talks at great length but never gets to the point)
 - Interpenetration of themes (rapid change to something completely different)
- **Thought Content**
 - Depersonalisation: feeling detached from oneself, feeling unreal (often with anxiety)
 - Derealisation: feelings of unreality of the external world
 - Spectrum: ideas → concerns → preoccupations → overvalued ideas → obsessions → delusion. Note different levels of conviction:
 - Over-valued idea: I think it but accept that others don't
 - Obsessional: I know it's not true but I can't get it out of my head
 - Delusional: I think that, and everyone else thinks that, and I don't believe them if they say they don't
 - Obsessional phenomena (see History Taking in Anxiety Disorders, page 422)
 - Delusions:
 - Evaluating delusions: Describe unusual statement, experience or event, decide if it is false, is there any cultural determination, classify it
 - Passivity phenomena/control:
 - Thought insertion: reports 'alien' thoughts
 - Thought broadcast: thoughts transmitted to other people
 - Thoughts spoken aloud: feels as if thoughts are audible to others
 - Thought echo: involuntary repetition of thoughts
 - Delusional mood
 - Delusional perception: perception + delusional interpretation
 - Paranoid delusions: Is anyone trying to harm you?
 - Referential delusions: have you noticed anything (eg on TV) that refers to you
 - Grandiose delusions, sexual delusions
 - Delusions of guilt, hypochondriasis, nihilism
 - Delusions of misidentification and misrepresentation: refers to the belief that people have been replaced by impostors
- **Suicidal and homicidal ideation**
 - See Suicide Assessment and Management, page 416
- **Perceptual Phenomena**
 - Illusions: misrepresentation of external environment – transformation without perception
 - Hallucinations:
 - *External* perception without any external stimulus. Hearing voices inside your head is not an hallucination – they should hear them as coming from outside their head

- Can be auditory, visual, olfactory, tactile or taste
- If auditory, clarify characteristics: sounds or voices, one or more voices, talk to you or to each other, give commands, do you recognise them, believe them
- **Cognition**
 - See also Cognitive Functions, page 122
 - Is defined by how we assess it!
 - Can test with Mental Status tests, etc
 - Observe alertness, attention and concentration (serial sevens, spell ‘world’ backwards, days or months backwards), orientation (time, place and person), memory, executive function, localised functions
 - Testing memory: short term – recollection at 5 minutes, recent memory – events over past several days (adapt to patient’s interests), remote memory – personal events, birth date, sequence of events [NB – this classification is really an artefact – it doesn’t correlate with how memory works]
 - Language: word finding, comprehension, reading, writing
 - Calculation: needed for getting change, paying bills
 - Visuospatial: dressing, finding way around, neglect, problem for driving
 - Visual perception: can’t recognise what they see
 - Personality change: usually exaggerates or ameliorates premorbid state: motivation, spontaneity, persistence, care, social conduct, quality of relationship, aggression
 - Problem solving ability
 - Consider in the context of ADLs (Activities of Daily Living) and Instrumental ADLs (eg using phone)
 - If confused may need to interview an informant
 - Patient will usually water down symptoms
- **Intelligence:** Vocabulary, previous and current performance
- **Insight and Judgement**
 - Awareness of their own mental condition, do they recognise the reasons for their difficulties
 - Full, partial, limited, grossly impaired
 - Base around 4 questions:
 - Are they aware of the phenomena others have observed
 - If so, do they recognise them as abnormal
 - If so, do they consider they are caused by mental illness
 - If so, do they need treatment
- **Rapport**
 - Sense of empathy, emotional response of interviewer to patient and patient to interviewer
 - Good, superficial, none
 - Easy to overestimate: key test is would they do something you asked if they didn’t want to. Can you predict future relationship

Suicide Assessment and Management

- Always screen all psychiatric patients for suicide
- Definitions:
 - Attempted suicide: self-inflicted harm intended to cause death
 - Parasuicide: Act intended to communicate distress not intended to cause death

Suicide History

- Overview:
 - Establish and maintain rapport
 - Evaluate for:
 - Suicidal thinking
 - Suicidal intent
 - Suicidal plans
 - Future orientation
 - Relevant mental status: including mood, drugs/alcohol, labile, impulsiveness, insight, etc
 - Assessment of risk factors
- Ideation questions:
 - Do you see a future for yourself?
 - Do you think a lot about death?
 - Have you ever considered harming yourself/wanted to end your life?

- What specifically have you thought about this? When did you start thinking this way?
- Have you talked to anyone about this?
- Do you want to die – or do you want others to realise how bad things are for you?
- Have you thought of a plan to kill yourself?
- Do you have the means?
- What has stopped you so far?
- Have you thought about the effect your death would have on family and friends?
- How do you feel about accepting help?
- How does talking about this make you feel?
- If can't ask the question directly, then 'what do you think about suicide', 'what would you do if it got that bad', 'how bad does it get... have you ever felt so bad that you wanted to end your life'
- Have you thought of hurting anyone else
- Past Suicide attempt(s):
 - What did you do?
 - When did you start thinking about suicide? Why did you think that?
 - When did you plan to do something? (ie was it impulsive or planned)
 - When did you start to action the plan? What triggered that (what was the final straw)?
 - Did you leave a note/say goodbye/wind up your affairs?
 - What stopped you going through with it?
 - How did you get to be in hospital?
 - Are you surprised to be alive? (ie did they genuinely think it was going to kill them)
 - Has anything changed in the things that made you try?
 - What did you feel about getting help?

Assessment of Risk

- Predisposing Risk Factors:
 - Present from birth or soon after:
 - Sex: Female more likely to try, male more likely to succeed
 - Genetic or congenital factors
 - Family History of suicide, psychiatric illness or substance abuse
 - Personality Traits (eg impulsiveness, perfectionism, hopelessness, low self esteem)
 - Risk Factors developed later in life:
 - Suicide Exposure
 - Psychiatric diagnosis: depression, substance abuse (esp. age 40 – 60) and schizophrenia show strongest correlation
 - Other illness
 - Previous suicidal intents: include factors listed above, type and frequency of ideation, etc
 - Environmental factors: separated, living alone, elderly, isolated, unemployed
 - High risk situations: eg young males
- Protective Factors: decrease risk:
 - Cognitive flexibility
 - Strong social supports
 - Hopefulness
 - Treatment of disorders
 - Responsibility for children
 - Are there other things that would stop them?
- Precipitating Factors: short term risk factors:
 - Humiliating/precipitating life event: job loss, move, separation, death, interpersonal problems
 - Post partum
 - Recent discharge from a psychiatric hospital: a high risk time
 - Current mood: depression increases risk significantly
 - Thoughts and expectations about the future. Very important to assessing overall risk. Is the future hopeless? If they have nothing to live for, suicide is easier
 - Mental State: mood, psychosis (→ impaired judgement, voices may tell them to do it, paranoia), judgement, impulsivity (be aware of effect of alcohol if person is sober when interviewed: when you drink, how do you feel afterwards)

- Current plan: detail, lethality (not how lethal it actually would be, but what did patient think would happen), fantasies (eg have they thought about other's reactions to their death), expectations of outcome (eg do they want to be found?) Availability of method
- High risk if:
 - Recent well planned attempt. Remains fixed on wish to die or refuses treatment
 - Patient has had thoughts about suicide and intends to act on them
 - If the patient is uncooperative and the assessment was incomplete
 - If the following are present: psych illness, significant stress, history of impulsivity or violence, family history of suicide

*Influence of community standards and norms on suicide**

- Individualism: you're a failure if you can't make it on your own
- Copy cat syndrome
- Expectations of achievement → individuals set high expectations and fail
- Community encourages the use of weapons
- Community demeans the poor → see themselves as unimportant
- Community encourages external locus of control → can't change anything ⇒ fatalism
- Community encourages/condones suicide in certain circumstances:
- People with certain conditions alienated, eg psych illness
- Minority culture alienated by enforced dominance of the dominant group's beliefs and values (hegemony) → alienation

*Management of Current Suicide Risk **

- For a high risk: emergency assessment (eg CAT team) followed by regular nursing assessment
- For lower risk in a GP setting (UK source):
 - Straight away:
 - Identify risk on notes in a way that won't be missed by you or other members of the team (eg note or sticker on summary sheet). Won't affect life insurance risk if insurance covers a mortgage or loan, or policy was taken out more than one year before. Suicide risk has no additional effect on premiums over and above the presence of depression
 - Don't give prescriptions with repeats – get them to come back for each script. Allows better monitoring and limits the amount of medication they hold at any time
 - Ensure adequate symptom relief of physical symptoms
 - Use a counselling approach: empathy, give feedback to clarify the patient's problems, provide advice if appropriate, etc
 - Further Actions:
 - Plan the next few days: especially if a weekend, or they have poor social supports. Should be detailed, and given to the patient on paper to take home. Should include contact with other people and things the patient enjoys
 - Ensure family member/responsible friend is available
 - Encourage use of informal supports: whom can they talk to. If there is nobody, why do they feel like this?
 - Use non-statutory Services: Lifeline, Youthline, Samaritans, community organisations, support groups, sports/hobby groups etc
 - Offer follow-up: opportunity to reassess patient, and provide further support
 - Consider referral to specialist care: Community Psychiatric Nurse, social worker, psychiatrist, psychologist, CATT
 - Afterwards:
 - Liase with other professionals
 - Discuss with another team member to review your risk assessment and management plan
 - Be aware of your own response: patients like these can cause considerable concern or evoke a strong emotional response

Interviewing Aggressive Patients

- Understanding why they are aggressive is important:
 - Poor anger control
 - Inappropriately managed
 - Overwhelmingly afraid
 - Most clients are afraid/confused by their own feelings

- Aggressive patients often try to change the ‘rules’ of the relationship between professional and client by trying to dominate. The interviewer must maintain the boundaries. If ‘rules’ are broken (eg threats, etc) → terminate the interview
- Interviewing tips:
 - Is it wise to interview them at all?
 - Get as much information about their history and current state before you start
 - Patients home most difficult environment
 - Ensure you and the client have direct access to a door
 - Appear confident!
 - Ensure there are no missiles (tea cups, ash trays)
 - Don’t sit eyeball to eyeball. Have the client in a low, soft chair
 - Have someone else sit in
 - Remain aware of clients body language
 - Negotiate breaks with the client – take a walk in the corridor
- Responses:
 - Set limits: “I can’t help you if you keep shouting”
 - Demanding patients: “Perhaps I need to know a bit more before I decide to...”
 - Reflection: “I can see that made you very angry”
- Evaluation:
 - Diagnose psychiatric disorder and assess mental state – especially paranoid states, command hallucinations, intoxicated, delirium, manic, depressed
 - History of violence, abuse, neglect
 - Who are intended victims
 - Emotional stressors
 - Quality of self control
 - External constraints on behaviour
 - Physical exam: old and new injuries
- Sedation: if drug sedation is necessary:
 - Haloperidol 2.5 – 5 mg PO/IV and Clonazepam 2 mg PO/IM. Effect takes up to 20 – 30 minutes. Repeat at 30 minute intervals to maximum of 3 doses
 - If you forcibly restrain or medicate someone, should initiate Mental Health Act (otherwise it constitutes common assault)

DSM IV Classification*

- Published 1994, replaces Diagnostic and Statistical Manual of Mental Disorders III and III-R

Diagnostic Axes

- Axis 1: Clinical Disorders eg major depression, adjustment disorder, schizophrenic disorder. Basis in medical model
- Axis 2: personality disorder or traits and mental retardation. More blurred distinction between person and pathology
- Axis 3: General Medical Conditions (physical disorders and conditions)
- Axis 4: Psychosocial and Environmental Problems (eg severity of psychosocial stressors, problems with primary support group, social environment, educational, occupational, housing, economic, access to health care system)
- Axis 5: global assessment of functioning (eg in the previous year)

Diagnostic Classes

Major Diagnostic Class	Examples of Disorders	Notes
Disorders usually first diagnosed in infancy, childhood or adolescence	Mental retardation, learning, Pervasive Developmental (eg Autistic), Attention Deficit and Disruptive Behaviour, Tic	

Delirium, Dementia and Amnestic and Other Cognitive Disorders	Delirium (eg due to GMC, substance intoxication or withdrawal), Dementia (eg due to Alzheimer's, Vascular, HIV, Head Trauma, CJD, Parkinson's, Huntington's). See Dementia, page 439 and Delirium, page 442	Some with specifiers for uncomplicated, with delirium, with delusions, with depressed mood
Mental Disorders due to a General Medical Condition (GMC) not elsewhere classified	Catatonic disorder or personality change due to ...	Most of diagnostic classes have a category 'due to a GMC' where the symptoms fit that class – eg Mood Disorder due to a GMC
Substance Related Disorders	For most substances there are [Substance] Use and [Substance] Induced (including psychotic, mood, anxiety etc)	Specifiers include: with/without physiological dependence, full/partial/sustained/early remission, with onset during intoxication/withdrawal
Schizophrenia and Other Psychotic Disorders	Schizophrenia, Schizophreniform, Schizoaffective, delusional, brief psychotic	Specifiers for Schizophrenia include paranoid, disorganized, catatonic, undifferentiated and residual types
Mood Disorders	Depressive (Major Depressive Disorder – single episode and recurrent – and Dysthymic), Bipolar (Bipolar I & II, cyclothymic)	Some have specifiers for severity, psychotic, remission specifiers, chronic, with catatonic/melancholic/atypical features, with post-partum onset, with seasonal pattern/rapid cycling
Anxiety Disorders	Panic (with/without agoraphobia), Agoraphobia (without panic), Specific phobia, social phobia, Obsessive-Compulsive, Post Traumatic Stress, Acute Stress, Generalised Anxiety	
Somatoform Disorders	Somatization, Undifferentiated Somatoform, Conversion, Pain, Hypochondriasis, Body Dysmorphic, Somatoform	
Fictitious Disorders	Fictitious Disorder with predominantly psychological/physical signs	Patients intentionally produce signs of medical or mental disorders and misrepresent their histories and symptoms. Have compulsive quality – but behaviours are purposeful and deliberate
Dissociative Disorders	Dissociative Amnesia, Fugue, Identity Disorder, Depersonalisation	Patient feels lack of unity in state of consciousness, confusion regarding their identity or multiple identities
Sexual and Gender Identity Disorders	Sexual dysfunctions (of desire, arousal, orgasmic, pain), Paraphilic (eg paedophilia), Gender identity	
Eating Disorders	Anorexia Nervosa (restricting or binge/purging type), Bulimia Nervosa (purging type, non-purging type)	
Sleep Disorders	Primary Sleep (eg dyssomnias and parasomnias) and Related to another mental disorder	
Impulse-Control Disorders Not Elsewhere Specified	Eg Kleptomania, Pyromania, Pathological Gambling	

Adjustment Disorder	With depressed mood, anxiety, mixed, disturbance of conduct/emotions	Where symptoms appear within 3 months of an identifiable stressor. Should not meet criteria for another axis I or II disorder, and excludes bereavement. A short-term maladaptive reaction to a stressor (ie impairs social/occupational function or causes distress).
Personality Disorders	See Personality Disorders, page 454	
Other Conditions that may be a focus of clinical attention	Psychological factors affecting medical condition (eg mental disorder/personality traits/maladaptive health behaviours affecting medical condition), medication-induced movement disorders, relational problems, problems related to abuse or neglect, Non-compliance, Malingering, Bereavement	

Using DSM Diagnoses*

- In DSM IIIR, “Delirium, Dementia and Amnestic and Other Cognitive Disorders”, “Mental Disorders Due to a General Medical Condition” and “Substance-Related Disorders” were grouped under the single heading “Organic Mental Syndromes and Disorders”. “Organic mental disorder” is no longer used as it implies other disorders don’t have a biological basis
- Qualifiers on Diagnostic codes:
 - Severity and course specifiers: mild, moderate, severe, in partial remission, in full remission, prior history of (ie have had full recovery)
 - Principal diagnosis/Reason for visit: if more than one diagnosis, which one was the principle one leading to admission/contact. Difficult to determine in dual diagnosis (substance related + non-substance related). Multiple diagnoses can be reported in multiaxial fashion
 - Provisional: when strong assumption that criteria will be met, but insufficient evidence currently available
- Not-otherwise specified used when:
 - Symptoms below clinical threshold or there is an atypical or mixed presentation
 - Symptom pattern is not included in DSM IV
 - When there is uncertainty about aetiology: eg whether it is due to a general medical condition, is substance induced or is primary
 - There is incomplete or inconsistent information
- Frequently used criteria – to exclude or suggest differential diagnoses:
 - Criteria have never been/are not met for...
 - Does not occur exclusively during the course of...
 - Not due to the direct physiological effects or a substance of a general medical condition – ie these have had to be considered and ruled out
 - Not better accounted for by...
- These criteria establish a hierarchy:
 - Disorders due to a general medical condition or substance-induced disorder pre-empts diagnoses of primary disorder with the same symptoms (eg Cocaine-induced mood disorder pre-empts Major Depressive Disorder)
 - A more pervasive disorder pre-empts diagnosis of a less pervasive disorder with a subset of the symptoms of the more pervasive disorder (eg Less pervasive disorder will have ‘Criteria have not been met for [the more pervasive disorder]’)
 - When there are very difficult diagnostic boundaries, use ‘not better accounted for’ to permit use of clinical judgement

Anxiety Disorders

Introduction

- Anxiety is usually normal, useful and protective. We learn to fear normal anxiety. Yerkes Dobson Curve (1908): moderate levels of anxiety can improve performance, but performance improvement plateaus and then falls with ↑ anxiety. Anxiety becomes debilitating if severe
- 4 clusters of responses:
 - Physiological: autonomic nervous system arousal, ↓sleep
 - Cognitive: perception of danger, threat, loss, hypervigilence
 - Affective: nervousness, fear, ↓concentration
 - Behavioural: fight or flight
- Anxiety disorders lead to:
 - Over activation of cognitions about personal danger
 - Underestimation of ability to cope
- Differential Diagnoses:
 - Exclude anxiety due to substance intoxication or withdrawal, or due to delirium
 - Physical conditions that cause or exacerbate anxiety (hyperthyroidism, hyperventilation – eg asthma, phaeochromocytoma, drug withdrawal, etc)
- Becomes a disorder when it causes significant distress or interferes with social or occupational functioning

History Taking in Anxiety Disorders

- Introductory Questions:
 - Are there currently things in your life that are causing distress/worry?
 - Are there things that have happened in the past that you can't stop thinking about?
 - How is your general health?
 - Any one else in your family had similar problems?
 - Most anxiety is part of a mixed anxiety/depression → importance of full psychiatric assessment
- General Anxiety
 - Would you describe yourself as a worrier? Do you worry about things that others don't worry about?
 - Do you sometimes make mountains out of molehills?
 - Do you ever find it hard to make decisions?
- Panic
 - Have you ever felt your heart pounding, felt frightened/afraid – what do you think was the cause?
 - Ever felt like a disaster was about to happen to you?
 - Do they occur when other people wouldn't feel afraid?
 - Do you avoid going out?
- Phobias/Avoidance:
 - Is there anything you would avoid if you could? What happens if you are unexpectedly faced with that object/situation?
 - Do you have worries/fears that prevent you from doing things you would like – or that others can do without difficulty?
 - Are you only worried if others will see you?
 - Are you worried/anxious in other settings?
- Obsessions and Compulsions:
 - Obsessive thoughts: Any thoughts that keep coming repeatedly into mind, even when you're trying to get rid of them?
 - Compulsive rituals:
 - Do you ever have to repeat actions over and over which most people would only do once?
 - Do you ever find yourself having to do things over and over again to get them just right?
 - Do you find yourself spending a lot of time doing things like cleaning or checking that everything is safe?
 - What happens if you are interrupted when doing these things?
- Trauma:
 - Do you still have recurrent memories of an upsetting event?
 - Do you have nightmares, have trouble sleeping, or feel jumpy?
 - Are there things that remind you of the event? Do you avoid these?

- How has the trauma changed the way you feel about the future, about what you enjoy?

Panic Disorder (with or without agoraphobia)

- Panic attack:
 - = Intense exacerbation of autonomic responses: discrete episode of intense dread, fear or doom
 - Sudden, abrupt onset
 - Symptoms include racing heart, trembling, SOB, nausea, fear of dying or losing control, going crazy. May have limited symptom attacks
 - Found across anxiety disorders and in non-anxious population
- Panic Disorder:
 - Recurrent and *unexpected* panic attacks. Situationally-bound panic attacks are characteristic of social or specific phobias, although situationally-predisposed panic attacks are frequent in Panic Disorder
 - Catastrophic misinterpretation of bodily sensations/mental events (eg has palpitations and thinks they're having a heart attack). Normal bodily sensations misinterpreted
 - High anticipatory anxiety: persistent worry about having additional attacks
 - Hyper-vigilance for feared sensations
- Agoraphobia:
 - = 'Fear of fear'
 - Fear of situation where escape may be difficult or embarrassing in the event of a panic attack
 - Avoid or endure with dread situations associated with panic attacks and feared bodily sensations
 - Characteristically involve clusters of situations including being outside the home, being in a crowd, on a bridge, in a car, train or bus
 - But fear NOT of the situation
 - Can occur with or without a history of panic disorder
 - In Panic disorder, the more agoraphobic avoidance there is, the worse the prognosis
- Differentiating from Social Phobia: in panic disorder, fear evaluation of what panic causes them to do (difficulty breathing, dizziness, weakness in limbs). In Social phobia, fear evaluation of what they do or say regardless of panic (blushing, sweating, trembling)

Specific Phobia

- Persistent and irrational fear and avoidance of a specific object or situation
- Leads to avoidance or intense anxiety on exposure to feared stimulus
- Fear recognised as excessive
- Disruptive to functioning (important – who cares about a snake phobia in NZ)
- Can also be anxious about fear reaction
- Usually related to animals (mice, snakes, spiders), natural environment (earthquakes), blood, injection or injury; specific situations (eg claustrophobia)
- Develop due to:
 - Direct conditioning through personal experience
 - Verbal or vicarious transmission (eg develop shark phobia after watching Jaws)
- Treatment:
 - Graded exposure
 - Cognitive restructuring
 - Physiological control: relaxation and medication (short-term only)

Social Phobia

- Fear of negative evaluation of performance in social situations. Fear they will do or say something embarrassing or humiliating. Fear visible anxiety symptoms
- Probability and cost of negative evaluation is over-estimated
- Early onset
- Leads to avoidance of social gatherings, public travel, etc
- Epidemiology: 6 month prevalence is 2 per 100, more females, onset in teens through to 35 → social isolation
- Aetiology: ?conditioned response, genetics

Generalised Anxiety Disorder

- Worry about worry: a meta-worry!

- Excessive and persistent worry about a number of areas of life including family, health, job, finances, etc
- Worrying dominant source of discomfort: spend half an average day worrying – most recognise they worry excessively about minor things but can't control it
- At least six-month duration, chronic fluctuating course
- Epidemiology: 2 – 8 % of the population, onset 20 – 40 years, male = female
- Symptoms: restlessness, feeling on edge, difficulty concentrating, mind going blank, irritability, muscle tension, sleep disturbance (esp difficulty getting back to sleep after waking, anticipatory thoughts while awake)
- Co-morbidity/differential: mood disorders, adjustment disorder (clearly identifiable stressor), panic attacks, socially anxious, low self-esteem, avoidant or dependent personality disorder
- Treatment:
 - Education
 - Training: relaxation, breathing control, structured problem solving, gradual confrontation of fears
 - Avoid sedatives: they will love them but will become dependent on them and underlying problems won't be fixed
 - Specialist referral if symptoms persist for a further 3 months

Obsessive Compulsive Disorder

- Upsetting and intrusive obsessional thoughts that are difficult to control (e.g. fear of contamination), leading to compulsive rituals (although can have rituals in the absence of obvious obsessions)
- Common compulsions: cleaning, checking, counting
- Treatment:
 - Hard to treat with CBT and antianxiolytics
 - Consider antidepressants
 - Some evidence of effectiveness of low dose risperidone (?may be delusional component)

Post Traumatic Stress Disorder (PTSD)

- Long lasting anxiety or memories about a severe traumatic event, including nightmares, flashbacks, anxiety, avoidance of reminders
- Diagnostic criteria:
 - Actual or threatened severely traumatic event where the response was intense fear, helplessness or horror
 - Event is persistently re-experienced: recollections, dreams, distress to cues of an aspect of the event
 - Persistent avoidance of stimuli associated with the trauma (triggers) and numbing of general responsiveness (eg ↓interest in activities, detachment, etc)
 - Persistent symptoms of increased arousal (eg difficulty sleeping, irritability, ↓concentration, hypervigilance)
 - Duration of > 1 month
 - Causes significant distress or impairment in social/occupational function
- Types:
 - Acute: duration of symptoms < 3 months
 - Chronic: duration of symptoms > 3 months
 - Delayed onset: onset > 6 months after stressor
- Differential: OCD, Acute stress disorder (resolves within 4 weeks), adjustment disorder, psychotic disorders, malingering

Acute Stress Disorder

- Distinguished from PTSD by duration < 1 month (i.e. short term reaction). Includes avoidance, fear of being alone, muscle tension, disbelief, problems with sleep, concentration and memory, guilt, self-doubt

Treatment of Anxiety Disorders

Cognitive Behavioural Therapy (CBT)

- Effective for most anxiety disorders
- Response more long lived than for drug treatment

- Includes: breathing retraining, deconditioning, cognitive restructuring, relaxation, graded exposure, desensitisation

Psychodynamic Psychotherapy

- Symptoms result from mental processes outside conscious awareness. Aim is to elucidate these
- Identify and alter core conflicts

Drug Treatment

- Benzodiazepines: may be useful for the short term or acute treatment of acute stress reactions. Due to tolerance and dependence, these are not useful for long-term use
- Antidepressants:
 - For severe panic disorder (with or without agoraphobia), TCA's (eg imipramine) are the medication of choice. Suppression of panic attacks may occur after 4 – 6 weeks. Minimum treatment usually 6 months. Maximum is 18 months. Use alternative therapies if it fails after this time
 - For OCD, clomipramine (a TCA) and SSRIs may be a useful adjunct to CBT. Help minimize compulsions and manage the depression often associated with OCD.
- Betablockers: Useful for the treatment of social phobia when performance anxiety is the main problem. These prevent noticeable symptoms (eg blushing or shaking), which are typically interpreted catastrophically by individuals. However, these drugs are not useful if the anxiety is more generalized

Benzodiazepines

- Mode of action: enhance GABA inhibition throughout the CNS
- GABA (gamma-amino-butyric acid) increases membrane Cl⁻ permeability → hyperpolarisation
- Binding affinity important in governing duration and degree of effect, in addition to elimination and dosage.

<u>Hypnotics</u>		T _{1/2}
- Ultra-short acting	Midazolam	1.5 – 2.5
	Triazolam	1.5 – 3
- Sleep sustainers	Zopiclone	4 – 6
	Loprazolam	6 – 9
	Temazepam	6 – 9
- Others	Lormetazepam	9 – 12
	Nitrazepam	25 – 35
	Flunitrazepam	15 – 35

<u>Anxiolytics</u>			
	Diazepam	32	Active metabolite T _{1/2} is 40 – 200 hours
	Chlordiazepoxide	12	Same metabolite as Diazepam
	Lorazepam	12	Pronounced withdrawal
	Oxazepam	8	Slow absorption
	Alprazolam	14	Panic disorders, antidepressant effects in anxiety states
	Clonazepam		Useful anticonvulsant activity

- Key pharmacodynamic differences:
 - Chlordiazepoxide and Diazepam: shorter elimination time than their active metabolites. Doses of benzos with active metabolites should be reduced in the elderly, especially if ↓renal function
 - Midazolam: often used as premed for procedures and GA – relaxes and amnesia
 - Zopiclone (Imovane): differs from BDZs and barbiturates, but has same actions (sedation, anticonvulsant, anti-aggressive and muscle relaxant). Binds to BDZ binding sites. Peak plasma conc. in 1 hour, T_{1/2} of 4 hours. At higher doses: hangover effect, memory disturbance, rebound insomnia, interaction with alcohol
- Metabolism:
 - Eg: diazepam → temazepam → oxazepam
 - Inactive conjugates excreted
- Adverse Effects:
 - Daytime sedation: with long acting BDZs where slow elimination leads to accumulation of drug and active metabolites

- Daytime agitation/irritability: with ultra short acting BDZs (triazolam, midazolam), especially in those with anxiety
- Psychomotor functional impairment: beware if driving or operating machinery
- Amnesia: with short acting BDZs
- Physical dependence: All BDZs are addictive
- CNS effects of BDZs all exacerbated by alcohol
- Broken sleep patterns are particularly common after withdrawal of hypnotics
- Discontinuation of long-term use must be gradual (2 – 3 months) never abrupt. Withdrawal similar to hyperadrenergic state – anxiety, tremor, ataxia, confusion, insomnia, nausea, seizures (especially with lorazepam). Withdrawal syndrome can be prolonged (ie months). Treating withdrawal: change to diazepam (greater dose flexibility), reduce dose by 10% every 2 – 4 weeks. Use counselling and relaxation
- Lorazepam as a hypnotic where insomnia is a complication of anxiety – but never just as a hypnotic
- See Treatment of Insomnia, page 534

Differentiating Anxiety and Depressive Symptoms

- Coexistence of anxiety and depressive symptoms is common:
 - Depressive symptoms occur secondarily especially in panic disorder, agoraphobia and OCD. If anxiety disorders go untreated → demoralised and progressive restrictions on function → depression
 - Anxiousness and irritability are seen in the majority of depressed patients, panic attacks may occur
- Differentiating:
 - GAD/Panic disorder don't usually have full range of vegetative symptoms
 - Anxious patients have trouble getting to sleep, depressed wake early
 - Anxious patients don't lose the capacity to enjoy things or be cheered up
 - Asking which symptoms came first can be helpful

	More Common in anxiety disorders	More common in depression	Common to both
Bodily	Difficulty falling asleep	Early waking, oversleeping	Sleep disturbance
	Tremor/palpitations	Diurnal variation	Appetite change
	Sweating	Chronic nagging pain	Non-specific bodily complaints
	Hot/cold flushes	Agitation or slowed behaviour	Fatigue
	Muscle tension	Loss of libido	Restlessness
	Nausea	Sadness, despair	Headaches
Feelings	Breathlessness	Guilt, hopelessness	Dry mouth
	Helplessness	Lack of motivation	Irritability
	“Stressed out/keyed up”	Lack of pleasure, flatness	Feelings of doom, anxious
Thoughts	Apprehension	↓Interest in normal activities, apathy	Dependent
	Expecting the worst	Slowed speech, thought processes, response times	Loss of enjoyment
	Catastrophic thinking	Suicidal thoughts	Tearful
Behaviour	Phobic avoidance of feared situations	Reduced mobility	Rapid mood swings
	Easily startled	Downcast expression	Difficulty with concentration
	Anxiety reducing rituals	Decreased socialising	Excessive worry
	Hyperferventilation		Indecision

Mood Disorders

Depressive Disorders

- References: Guidelines for the Treatment and Management of Depression by Primary Healthcare Professionals, National Health Committee, September 1996

Diagnosis of Major Depressive Disorder/Episode (MDE)

- Handy mnemonic:
 - **S:** Sleep
 - **A:** Appetite and weight
 - **D:** Dysphoria and anhedonia
 - **F:** Fatigue
 - **A:** Agitation/retardation
 - **C:** Concentration
 - **E:** Esteem
 - **S:** Suicide
- DSM IV criteria:
 - 5 or more of the following present during the same 2-week period and represent a change from previous functioning. At least one symptom must be depressed mood or loss of interest/pleasure [NB exclude symptoms clearly related to a general medication condition, delusions or hallucinations]. Note duration and persistence of each symptom, and compare to normal:
 - Depressed mood, most of the day, nearly every day (either self report or observed by others)
 - Markedly diminished interest or pleasure in all, or all most all, activities (exclude grief reaction)
 - Significant weight loss/gain or ↓/↑ in appetite (exclude cancer, Tb, hypothyroid)
 - Insomnia/hypersomnia nearly every day (exclude sleep apnoea)
 - Psychomotor agitation or retardation (excessive repetitious and pointless motor activity that is associated with feelings of tension. Needs to be observable, not just felt). Eg have you been fidgety/restless or felt 'stuck in the mud' or in slow motion?
 - Fatigue or loss of energy nearly every day
 - Feelings of worthlessness or excessive or inappropriate guilt nearly every day. Eg how do you feel about yourself, have you blamed yourself for things, do you feel guilty?
 - Diminished ability to think or concentrate, or indecisiveness, nearly every day
 - Recurrent thoughts of death, suicidal ideation without a plan, an attempt or a plan
 - Symptoms do not meet criteria for a mixed episode
 - Symptoms cause significant distress or impairment in social and occupational functioning. Eg what difficulties have all these symptoms caused?
 - Exclude depression if symptoms:
 - Are due to physical illness, medication or street drugs
 - Occur within 2 months of significant bereavement (except if marked impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or psychomotor retardation). Key difference between grief and depression is whether they themselves feel worthless or not
- Also review risk factors:
 - Prior history of major depressive episode or suicide attempt. Previous episode → 50% lifetime risk of recurrence
 - Family history of mood disorder or suicide attempts. If no family history then lifetime risk 10 – 20%. If heavy genetic loading this may double the risk (very polygenic)
 - Chronic or severe physical illness (may → demoralisation and hopelessness)
 - Concurrent substance abuse
 - Recent stressful life events and lack of social support (stress should not be used to 'explain away' symptoms, stress may precipitate a major depressive episode)
 - Childhood trauma, abuse, parental conflict or deficient parental care
 - Recent childbirth or other family changes (eg divorce, children leaving home)
 - Responsibilities for caring for others (eg elderly relatives)
- Differentials:
 - Substance abuse
 - Other psychiatric disorders, eg anxiety, eating and adjustment disorders, personality disorders, somatization
 - Dementia in older people (a key differential is memory)
 - General medical conditions and medication. Drugs affecting mood:
 - Steroids: on 20 mg 1.3% get depression, on 80mg 20% get depression
 - Lipid soluble β blocker
 - New drug affecting P450 metabolism and ↑ plasma conc. of existing drug

- Grief reaction. Depressive symptoms common during periods of grief. Usually begins within 2 – 3 weeks of bereavement and usually resolves without treatment – although supportive counselling/practical help may be indicated
- In children and adolescents, feelings of guilt, emptiness, self-dislike and failure are common – but are underreported by parents, who may instead report a decline in behaviour or academic performance
- Can use questionnaires: e.g. GHQ (General Health Questionnaire) or CES-D – useful either for screening or in borderline situations – gives something to discuss with patient
- Little point in trying to separate exogenous from endogenous depression (often a chicken & egg situation). It's usually multifactorial – regardless of cause may well need a multi-factorial approach to management

Subgroups

Subgroup	Essential Features	Implications
Psychotic Depression	Hallucinations and/or delusions	More likely to become bipolar than non-psychotic types (esp under 25s). May be misdiagnosed as schizophrenia
Melancholic Depression	Loss of pleasure and lower mood (typically in morning), marked psychomotor retardation or agitation, significant weight changes and inappropriate guilt	Indicative of more severe depression. More likely in older patients. Maybe misdiagnosed as dementia if cognitive impairment or psychomotor retardation are prominent
Atypical Depression	Various: overeating, oversleeping, weight gain, mood still reactive to events, anxiety symptoms, heaviness in arms & legs	Common in younger people. May be misdiagnosed as a personality disorder.
Postpartum Depression	See page 430	
Postpartum Psychosis	See page 430	
Seasonal Affective Disorder	Typically onset in autumn and remits in spring. Summer episodes may also occur	Recurrent

Epidemiology and Aetiology

- Lifetime risk of depression in women is 20%
- Female: Male is 2:1, but in younger cohorts an ↑ in male depression is bringing the ratio down to 1.6:1. This is not an artefact of help-seeking behaviour
- Rate is increasing
- Variety of theories:
 - Biological (eg neurotransmitter dysfunction)
 - Freud: unresolved early childhood events resurrected by similar events in later life
 - Bent (?): Cognitive triad: people feel helpless → hopeless → worthless. Selective abstraction – extrapolate from one event to everything. Treatment: Uncover underlying schema. Then challenge faulty thinking (is it always that bad?), challenge automatic thoughts

Assessment

- Cultural issues:
 - Different cultures have different views on the cause and treatment of depression.
 - Appreciating the cultural perception of the individual → better therapeutic relationship and ↑ effectiveness of intervention.
 - Consider referral to culturally appropriate service.
 - Cultural issues may affect the way the interview is conducted. Eg if Maori, establish initial rapport before asking name and personal information, don't make eye contact when discussing sensitive information, a family member speaking on a patient's behalf is not being dominating, etc
- Assessment of severity: Use the number of DSM IV criteria met or severity rating scales. Allows classification into mild, moderate and severe. Can be used to monitor progression of treatment and relapse
- Assess duration: (> 6 months, > 24 months)
- Refer to specialist services when:
 - There is serious risk of suicide (or harm to others, especially younger children)

- The child is under the age of 13 years
- There are psychotic symptoms or bipolar disorder (depressed phase)
- The diagnosis is unclear and needs further evaluation
- Melancholic features are so severe that they are unable to look after themselves and have inadequate community support
- There are complex problems (eg poor relationship, another psychiatric disorder)
- Considering enhancing antidepressants with mood stabilisers (eg lithium)
- Failure to respond to recommended treatment within 12 weeks

Treatment of Major Depressive Disorder

- Fundamental to treatment is:
 - Establishing positive therapeutic relationship
 - Developing shared understanding of problems
- Safety: suicide risks common (lifetime risk 25 – 50%). Higher in delusional Major Depressive Episode. Consider safety of others, especially if psychotic beliefs or Postpartum Depression
- Lifestyle changes that have been shown to be effective: stress management, ↓alcohol and drugs, good sleep patterns, a balanced diet, and physical exercise
- Role of family, friends and self help groups important in maintaining a supportive environment
- Education (over time):
 - Depression is an illness not a weakness.
 - Treatment is effective and recovery is normal.
 - Recurrence is possible so compliance is important. However, sometimes there is only partial remission between episodes. Recognition of warning signs and seeking early treatment will reduce severity
- Psychological treatment:
 - Indicated if:
 - Person with mild to moderate chooses this as first line
 - If partial response to drugs at week 6 or 12 and residual symptoms are largely psychological
 - There are continuing issues/cognitive beliefs that ↑ the risk of relapse
 - Not as sole treatment in severe, psychotic or melancholic depression
 - Promoting change: behaviour, thoughts, emotion
 - Different therapies:
 - Cognitive behavioural therapy (See Cognitive Behavioural Therapy (CBT), page 457)
 - Problem solving therapy (See Problem Solving Therapy, page 457)
 - Interpersonal therapy
 - Hypnotherapy
 - Psychoanalysis
 - Transactional analysis
 - Martial or family therapy
- Drug treatment: See Antidepressant and Mood Stabilising Medication, page 431
- Electroconvulsive Therapy (ECT):
 - Relieves symptoms in 80% of all severe depressions (not just those resistant to medication)
 - Indications:
 - Psychotic depression
 - Depressive stupor (severe psychomotor depression)
 - Severely suicidal
 - Previous good response to ECT
 - Risks: little risk of brain injury – risks are those of a general anaesthetic. Most troubling side effect is memory loss. Anterograde loss is usually short lived. Some retrograde loss may be permanent
 - Response is proportional to length and quality of seizure. Usual course is about 6 cycles. If no response after 12 cycles then stop
 - Also need to establish on an antidepressant that they haven't failed on
- Monitoring treatment in primary care:
 - Check for treatment response, side effects, and alteration in stressors or supports
 - If severe, monitor twice weekly by consultation and phone, if mild then weekly
 - Assess response in week 6

Postpartum Mood Disorders

	Frequency	Symptoms	Course	Risks & Treatment
Postpartum Blues	50 – 80%	Weepiness, anxiety, irritability, poor concentration, euphoria	3 – 10 days post partum	Treatment: support, reassurance, monitor. Function not usually affected
Postpartum Depression	10 – 15 %	Common symptoms: anxiety, spontaneous crying, lack of interest in baby, guilt, hard making decisions, panic attacks, especially insomnia & fatigue. Mood may fluctuate. Obsessional thoughts. Suicidal ideation.	Not before 3 rd day. 80% onset within first 6 weeks. Gradual onset – may not be apparent until 4 th or 5 th month. Duration 6 – 9 months.	30 – 50% chance of recurring in next postpartum period. May approach 100% if history of mood disorder and previous postpartum depression. Treat as for MDE.
Puerperal or Postpartum Psychosis (No criteria in DSM4)	0.1 – 0.2 %	Severe, labile (unstable) mood. Obsessional thoughts (eg about baby's health). Suicidal ideation. Delusions (eg baby defective), suspicious, persecuted, confused	Acute onset < 14 days post partum. Good prognosis. Duration 2 – 3 months	30 – 50% chance of recurring in next postpartum period Treatment: Ensure safety. Antidepressant, Lithium, antipsychotic. Consider ECT early – safe and effective.

- Screen at post-natal check up (6 weeks) using Edinburgh Postnatal Depression Scale (EPDS), but still needs careful clinical assessment
- Differential: hypothyroidism (more common post-partum), recurrence of previous psychiatric illness, initial presentation of a psychiatric illness (eg schizophrenia or anxiety disorders – postpartum period increases risk), adjustment disorder with depressed mood
- Possible aetiological factors:
 - Stress of delivery, difficult pregnancy
 - Lack of sleep
 - Hormonal
 - Isolation, lack of support
 - Internal conflicts about role as mother: motherhood idealised or devalued, very difficult adjustment in role, powerless, dependent, alone, may have had unrealistic expectations, etc
 - May not have wanted to be pregnant, may now feel trapped in unhappy situation (eg relationship)
 - Cultural factors: cultures vary in support offered (eg by extended family) to new mother, in pressures to return to work (variable maternity leave policies), differing attitudes to female children, etc.
- Considerable overlap in the risk factors for major depression, post-partum depression, inadequate parenting and child abuse
- Treatment:
 - Check whether drugs enter breast milk.
 - Indications for antidepressants similar for those for other mood disorders
 - If agitated or anxious, more sedating antidepressants are appropriate (eg imipramine) or even small doses of antipsychotics
- Long term effect of postnatal depression on child development: disturbances in mother-infant relationships (eg attachment), impaired cognitive and emotional development in later infancy, and ↑ risk of longer-term behavioural and social development of the child. These factors compounded by indices of socio-economic adversity, which are risk factors for these outcomes and for depression. So good initial diagnosis and treatment important

Dysthymic Disorder

- Diagnostic criteria:
 - Depressed mood for most of the day, for more days than not, **for at least 2 years**
 - Other depressive symptoms
 - But not a major depressive episode, no manic, hypomanic or psychotic features, no substance abuse or GMC

- Differential from Major Depressive Disorder:
 - Difficult as differences in onset, duration, persistence and severity are not easy to retrospectively evaluate
 - Major depression often has a more marked contrast from normal. In dysthymic disorder, low mood is less easily distinguished from person's normal function
 - If major depressive episode on top of existing dysthymic disorder, then may recover more quickly than normal from the major depression, but are at significantly higher risk of relapse with faster cycles
 - Treatment: antidepressants for up to three years together with appropriate life skills training and psychological therapy

Bipolar Depression (Manic-Depression)

- Affects 1% of the population (35,000 New Zealanders)
- Genetic predisposition:
 - No family history then risk is 1%
 - One parent then risk is 20%
- Symptoms:
 - Manic Phase: elation, pleasure, energy, racing thoughts, invincible, grandiose (\uparrow self esteem), irritable, aggressive, lack of judgement (eg reckless driving, spending sprees, sexual indiscretion)
 - Depressive Phase: same symptoms as for major depressive episode
- History questions for mania:
 - How do you feel about yourself?
 - Do you feel that you are special?
 - Have you needed less sleep?
 - How much have you been spending lately
- Classifications of Bipolar Depression
 - Mixed Episode: rapidly alternating mood – at least 1 week in which the criteria are met for a manic episode and a MDE nearly every day
 - Bipolar 1: one or more manic or mixed episodes, usually accompanied by MDEs
 - Bipolar 2: one or more MDEs accompanied by at least one hypomanic episode
 - Cyclothymia: At least 2 years of numerous periods of hypomanic symptoms and depressive symptoms that don't meet criteria for mania or MDE (cf Dysthymia)
- Mood stabilising medication:
 - Lithium carbonate (requires regular blood tests. Can they get to the lab?)
 - Carbamazepine (Tegretol)
 - Sodium Valproate (Epilim)
 - All have similar efficacy, Lithium most common
 - Antipsychotic or tranquillising medication often added during early stages to reduce agitation and hyperactivity
 - Antidepressant medication can be used during depressive phase (although therapeutic delay a problem), and withdrawn gradually when it resolves. If used in isolation without a mood stabiliser, may precipitate a manic phase as the depression lifts
- Can be very stressful on relationships for family members

Lithium

- Indication: In bipolar, but also recurrent unipolar. Not good for acute mania – takes 2 – 4 weeks, full response may take 6 months
- Pharmacokinetics:
 - Variable absorption. $T_{1/2}$ is 18 hrs in young, 26 hours in elderly. Excreted unchanged. 80% reabsorbed in proximal tubule
 - Renal clearance of Li reduced by *diuretics, NSAIDs, theophylline, caffeine, dehydration, low sodium*
 - Clearance related to tubular sodium load. If \uparrow Na excretion (eg loop and thiazide diuretics) then \downarrow Li excretion.
 - ACE inhibitors $\rightarrow \uparrow$ Li levels
- Monitoring:
 - Narrow therapeutic range for maintenance treatment: 0.4 – 0.8 mmol/l
 - Therapeutic drug monitoring for Li is mandatory when: side effects, relapse of symptoms, serious illness (eg dehydration), dose adjustment
 - Check thyroid and renal function before starting

- Monitoring every three months should include Li levels, electrolytes, thyroid function
- Monitor 12 hrs after immediate release, 5 hrs after slow release. Slow release preparations prevent peaks in plasma conc. (\rightarrow nausea, headache)
- Side Effects:
 - Minor symptoms such as tremour and nausea do not predict serious toxicity:
 - Tremor (especially elderly), nausea, loose bowel motions (especially if levels $> 0.8 \text{ mmol/L}$)
 - Polyuria (especially when starting)
 - Weight gain: approx 4 kg
 - Pretibial oedema
 - Metallic taste
 - Dose dependent adverse effects:
 - 1.5 – 3 mmol/l – ataxia, weakness, drowsiness, thirst, diarrhoea
 - 3 – 5 mmol/l – confusion, spasticity, convulsions, dehydration, coma, death
 - Dose independent: hypothyroidism (reversible in early stages), nephrogenic diabetes insipidus, ECG changes & arrhythmias, acne, GI disturbance, weight gain, \downarrow bone calcium
 - Long term Li does not change GFR or lead to renal failure

Antidepressant and Mood Stabilising Medication

- Indications for antidepressant use:
 - Generally not indicated for mild disorder until monitoring, lifestyle changes and psychological therapies have been attempted
 - Indicated for mild disorder when there is a history of severe episodes or in dysthymic disorder which is persistent and disabling
 - For moderate, TCA or SSRIs equally indicated: depending on contraindications and toleration of side effects:
 - SSRIs where severe heart disease, significant anticholinergic problems, and where alertness is important
 - Amitriptyline and imipramine cause the most postural hypotension and AntiACh effects of the older TCAs. Good where sleep disturbance is a major symptom
 - For severe with melancholic features, TCAs at sufficient dose if side effects can be tolerated. Otherwise SSRIs (caution in pregnancy – risks not fully known)
 - If psychotic, use antipsychotic or consider ECT
 - For moderate and severe, continue for at least 9 months. If more than one recent episode, consider continuing for up to 3 years
 - During pregnancy: More experience with TCAs (ie more confident effects on fetus will be minimal)
 - Maintenance therapy at full therapeutic dose should be considered if high risk of relapse
 - Li in relapsing bipolar and as possible adjunct in relapsing unipolar depression
- Mode of action of antidepressants:
 - Increase concentration of noradrenergic or serotonin neurotransmitters in the synaptic cleft.
 - Leads to adaptive changes eg down regulation of post synaptic β and 5HT2A receptors (hence therapeutic delay)
 - Older agents also had antimuscarinic and antihistaminic activity
- Starting and stopping:
 - Onset of effect can take 1 – 2 weeks, with full effect possibly not for 4 – 8 weeks
 - Dose-escalation is a trade-off between desire to reach therapeutic plasma levels as soon as possible while avoiding side-effects
 - Rapid cessation of any antidepressant can cause a withdrawal syndrome from a few days resolving in about 4 weeks. Taper off treatment. (?Less risk with SSRIs due to longer $T\frac{1}{2}$)
- Drug treatment has similar outcomes as psychological or combination treatment (BMJ 2000, 320: 27-30)

Tricyclic Antidepressants

- Examples: Amitriptyline, Imipramine, Doxepin, Nortriptyline (least orthostatic hypotension)
- Action: Inhibit reuptake of serotonin, noradrenaline or both
- Use:
 - Clinical response takes 10 – 14 days. Start with low dose and increase gradually.
 - Relapse common \Rightarrow continue for 6 months
 - Not in acute MI. Care if suicidal (overdose risk), mania, and variety of medical conditions

- Pharmacokinetics:
 - Very low Vd \Rightarrow dialysing for overdose ineffective
 - Long T $\frac{1}{2}$ \Rightarrow once a day dose possible, but may split dose to reduce the dose dependent anti Ach effects
 - Well absorbed. Extensive 1st pass metabolism to active metabolites.
 - Individual variability in metabolism \rightarrow difficulty setting dose.
 - Protein bound and large Vd.
 - Long T $\frac{1}{2}$ (15 – 30 hours), prolonged in elderly. Can be given once daily, but high peak plasma levels \rightarrow ↑side effects
- Side effects of TCAs: Tricyclics
 - Inhibit reuptake of:
 - 5HT \rightarrow anorexia, nausea, vomiting
 - NA \rightarrow tremors, tachycardia, erectile and ejaculatory dysfunction, insomnia
 - DA \rightarrow less significant
 - Block:
 - Ach \rightarrow dry mouth, urinary retention, blurred vision, constipation, tachycardia
 - Alpha 1 \rightarrow postural hypotension (persistent in elderly). Delay in ejaculation and erectile dysfunction
 - H1 \rightarrow sedation, weight gain
 - Other: Possible convulsions, ataxia, manic reactions, respiratory depression, bundle branch block, delirium. Arrhythmias/arrest in overdose
 - There are marked differences in side-effect profile between people and between drugs
- Withdrawal of TCAs:
 - GI: nausea, vomiting, abdominal cramps, diarrhoea
 - General somatic distress: lethargy, flu-like symptoms, headache
 - Sleep disturbance: insomnia, abnormal dreams including nightmares
 - Affective symptoms: anxiety, agitation, low mood
 - Less commonly: movement disorders, mania, hypomania, arrhythmias, tachycardia, ventricular ectopic beats
- TCA Drug interactions:
 - Alcohol potentiates sedation
 - Potentiation of antimuscarinic drugs, adrenaline, noradrenaline and pseudoephedrine
 - Anticholinergics: worsening of dry mouth, tachycardia, constipation, urinary retention, blurred vision, narrow angle glaucoma
 - Antihistamines, alcohol, anxiolytics: sedation (especially bad if driving)
 - Anaesthetics: arrhythmias and hypotension
 - Diuretics: postural hypotension
 - Antihypertensives: increased hypotensive effect
 - MAOIs: CNS excitation (look like they're thyrotoxic) and hypo-hypertension
 - SSRIs: Fluoxetine inhibits TCAD plasma levels/side effects
- Tricyclic Overdose:
 - Gastric lavage up to 18 hours post ingestion, charcoal, support respiration
 - Symptoms:
 - Anticholinergic signs: rapid pulse, dilated pupils
 - Cardiac: hypotension (α 1 blocking effect), arrhythmia (PR and QRS intervals)
 - Neurological: CNS, seizures, sedation, extrapyramidal syndromes
 - Respiratory: depressed CNS
 - Other: ileus and urinary retention
 - Sodium bicarbonate if life threatening arrhythmias, lignocaine for ventricular rhythms, magnesium. Beware use of physostigmine

SSRIs

- = Selective Serotonin Re-uptake inhibitors
- Action: Initially inhibit 5HT re-uptake. Long term, normalise 5HT1A and 5HT2 receptor density
- Pharmacokinetics: Well absorbed. Fluoxetine: active metabolite with T $\frac{1}{2}$ of 7 – 10 days. Others, T $\frac{1}{2}$ of Use: Therapeutic delay of 3 – 4 weeks. Can be given once a day
- About 24 hours, inactive metabolites

- Examples: Fluoxetine/Prozac, Paroxetine/Arapax, Citalopram (popular in the UK, not subsidised in NZ)
- SSRI Side effects:
 - Common:
 - Nausea 23%, headaches, diarrhoea 15%, anxiety (early in treatment, Fluoxetine more stimulant than Paroxetine), nervousness and insomnia 25%
 - Sexual dysfunction is common
 - Weight loss 4%
 - Less common:
 - Postural hypotension uncommon, but can be significant
 - Sweating, constipation, weight loss, EPS (akathisia, dystonias, tardive dyskinesia), hyponatraemia
 - Less affinity for aminergic receptors than TCAs
 - Lack of cardiac toxicity in overdose (significantly less than TCAs) – no effect on QTc
 - May precipitate serotonin syndrome: fever, tremor, myoclonic jerks, convulsions, diarrhoea, hyper-reflexia. Can be fatal. NEVER prescribe MAOIs and SSRIs
 - Care in variety of medical conditions
- Withdrawal of SSRIs: Withdraw slowly
 - GI: nausea, vomiting, diarrhoea, loss of appetites, abdominal pain, abdominal distress
 - General somatic distress: lethargy, flu-like symptoms
 - Sleep disturbance: insomnia, abnormal dreams including nightmares and decreased need for sleep
 - Affective symptoms: irritability, anxiety symptoms, agitation
 - Problems with balance: dizziness, vertigo, light-headedness, ataxia
 - Sensory abnormalities: paraesthesia, numbness, blurred vision/diplopia, visual lag
- Interactions of SSRIs:
 - Cytochrome P450 inhibition is a major risk factor: 2D6, 3A4, 2C – depending on drug type (eg Sertraline, Fluoxetine, Paroxetine)
 - 2D6: 10% Caucasians lack it
 - Inhibited by Fluoxetine, Sertraline and Paroxetine
 - TCAs plasma levels/effects ↑ by 50 – 400%
 - Haloperidol levels may be increased (Fluoxetine most potent at this)
 - 2C:
 - Phenytoin (up to 3 fold ↑)
 - Tolbutamide (hypoglycaemia with Sertraline)
 - Warfarin (↑ INRs on sertraline and paroxetine)
 - Diazepam (sedation with fluoxetine)
 - 3A4: involves many drugs, including triazolam, carbamazepine, erythromycin, terfenadine, midazolam. Potential for multiple interactions
- Nefazodone: An SSRA + 5HT2 antagonist. Not really an SSRI but similar action. Side-effects similar to TCAs: nausea, dry mouth, dizziness, constipation, blurred vision
- St John's Wort (Hypericum): inhibits re-uptake of 5HT, noradrenaline and dopamine. In correct dose is as effective as imipramine and significantly better than placebo. Adverse effects include nausea, but no antimuscarinic effects. With SSRI can cause mild serotonin syndrome. Mild enzyme inducer → ↑ metabolism of warfarin, and others

MAOIs (Monoamine Oxidase Inhibitors)

- Action:
 - Inhibits MAO, which breaks down 5HT and noradrenaline intracellularly. Isoenzymes in gut and liver (type A) and brain (type B) all inhibited
 - MAO-A (intestine, placenta): selectively oxidises NA, Ad and 5HT
 - MAO-B (platelets): oxidises phenylethylamine
 - Tyramine and Dopamine are substrates for both forms
- Types:
 - Standard MAOIs are irreversible. Eg Tranylcypromine, Phenelzine inhibit MAO-A. Selegiline (deprenyl) irreversibly inhibits MAO-B
 - Reversible inhibitor of MAO - A (RIMA), eg Moclobemide. Similar efficacy to TCAs and SSRIs. Given 3 times a day
- Use:
 - MAOIs rare as first line treatment. Use moclobemide instead

- Therapeutic delay for about a month
- Pharmacokinetics:
 - MAOIs: Well absorbed. Pharmacokinetics of little importance as kinetics depends on irreversible inhibition
 - RIMAs: Well absorbed. Wears off quicker than MAOIs. Fairly extensive 1st pass metabolism. 50% protein bound. Large Vd. T½ is 2 hours
- MAOI side effects. MAO inhibition → ↑ catecholamine levels:
 - Postural hypertension, urinary hesitancy, dry mouth, blurred vision
 - Impotency and anorgasmia 20%
 - Hepatotoxicity
 - Carpal tunnel like syndrome
 - CNS: agitation, anxiety, hypomania, headache, tremour,
 - Other: weight gain, insomnia.
 - Contraindicated/caution in variety of medical conditions
- Food interaction: tyramine rich foods:
 - Foods include avocado, aged cheddar, yoghurt, meat, red wine, chocolate, yeast extracts, some beers, vegemite, pickled herrings, chicken liver.
 - Tyramine a precursor to dopamine and nor-adrenaline. Normally tyramine metabolised in gut by MAO.
 - If inhibited → ↑ plasma conc. → ↑ noradrenaline → hypertensive crisis, subarachnoid haemorrhage, etc. Adrenaline breaks down to HMMA, which can be detect in the urine.
 - RIMAs have 10 times the capacity to metabolise tyramine (ie food much less of an issue)
- Drug Interactions:
 - Sympathomimetics, including indirectly acting sympathomimetics (eg in cough mixtures such as ephedrine): hypertension
 - Opiod analgesics: hypo/hypertension
 - Antihypertensives: loss of effect, exacerbation of hypertension
 - Anticholinergics: increased effects
 - SSRIs and pethidine: serotonergic syndrome (fever, sweating, convulsion, confusion)
 - L-Dopa: dopaminergic crisis
 - Potentiate oral hypoglycaemics (sulphonylureas)
- MAOI Overdose:
 - Symptoms: CNS hyperactivity, sweating, hyperthermia, tachycardia, hyperventilation, muscle rigidity +/- dystonic facial and limb movements
 - Treatment: α and β blockers, chlorpromazine + supportive management

Psychotic Disorders

- Psychosis = distortion or loss of contact with reality (eg delusions, hallucinations, thought disorder) *without* change of consciousness (cf Delirium)
- See Mental State Examination, page 414, for definitions and history questions relating to psychosis
- Diagnostic hierarchy for psychosis:
 - Organic psychoses: Delirium, dementia, other organic disorders
 - Functional psychoses: Mania, schizophrenia, depression
 - Non-psychotic disorders: anxiety disorders, abnormal illness behaviours
 - Personality disorders

Types of Psychotic Disorder

- Brief Psychotic Episode: symptoms have lasted > 1 day but < 1 month, and the patient has returned to pre-morbid functioning in that time. Uncommon. May develop in response to severe psychosocial stressor. More common in personality disorders (histrionic, narcissistic, paranoid, schizotypal, borderline)
- Schizoaffective Disorder: manic or depressive syndrome develops concurrently
- Delusional Disorder: non-bizarre delusions present for 1 month without any other symptoms of schizophrenia
- Schizophreniform Disorder: duration of > 1 month but < 6 months (may progress to schizophrenia)
- Schizophrenia

Schizophrenia

- Key features: positive symptoms, negative symptoms, *deterioration in functioning over time*
- It is not a split personality (ie multiple personality disorder)
- Epidemiology:
 - 1% (30,000) NZers have or have had schizophrenia
 - Median age of presentation: males 19, female 24
- Symptoms:
 - Positive symptoms:
 - Hallucinations: comes from external space. Typically 2nd or 3rd person auditory hallucinations
 - Delusions: fixed false beliefs out of cultural context
 - Thought disorder: 'loss of syntax', non-linear. Different to confusion or incoherence
 - Bizarre and/or disorganized behaviour: eg aggressive, disinhibited, violent (often in 'self-defence' if paranoid - rare but possible).
 - Catatonic behaviour: if long term, untreated psychosis then may assume odd positions, waxy flexibility, totally unresponsive
 - Negative symptoms:
 - Deficiency of mental function - Cognitive symptoms: difficulty concentrating, learning, hard to assemble thoughts. Not a decline in intelligence. Will still remember. Don't try to pull the wool over their eyes
 - Alogia: poverty of speech or speech content
 - Affective flattening: including reduced intensity of emotional response
 - Anhedonia: don't care about their lack of interest, cf depression where they want to enjoy themselves but can't
 - Asociality - uninterested in the company of others, unresponsiveness, withdrawal
 - Prodrome = gradual change prior to first episode of frank psychosis. Look for:
 - ↓Concentration, attention drive, motivation
 - Depression, anxiety
 - Sleep disturbance
 - Social withdrawal, suspiciousness
 - These are common in adolescence: you're looking for marked change over previous function
 - Associated problems:
 - Suicide in 10 – 15%
 - Lack of insight (→ non-compliant with medication)
 - Substance abuse: co-morbid problem, ?self medication
 - Depression in schizophrenia: diagnosed as Depressive Disorder NOS
 - Neurological symptoms: abnormalities in balance, proprioception, graphesthesia, disorder in smooth eye pursuit, decreased blinking
 - EPS (extra-pyramidal side effects) in 20% of drug naïve people suffering from schizophrenia (⇒ it's not always due to drugs)
 - Subtypes:
 - Paranoid: delusions, hallucinations
 - Disorganized: disorganized speech, behaviour, flat/inappropriate affect
 - Catatonic: motor immobility, excessive motor activity, negativism, stereotypies (repeated monotonous movements), echolalia, echopraxia
 - Undifferentiated
 - Residual
 - Aetiology:
 - Multi-factorial: don't know about relative loadings for predisposing and precipitating factors
 - Genetic: one parent affected → 5% chance, two parents → 45% chance, sibling affected → 10% chance
 - Neurodevelopment: brain injury at birth and perinatal complications (eg low Apgar), born in winter, ?viral influences. Insults at this age not causal – but some correlation
 - Social causation: eg Shift and Drift or Breeder theory to try and explain higher incidence in lower socio-economic groups, Expressed Emotion theory (a lot of critical comment and high expectations from parents)
 - Vulnerable personality: schizoid, schizotypal, paranoid
 - Head injury
 - Precipitating factors: life events, drug abuse, etc

- Differential Diagnosis:
 - Psychiatric disorders: Bipolar (manic phase), Major Depression with Psychotic Features, Brief psychotic disorder, schizopreniform disorder, schizoaffective disorder, delusional disorder, depersonalisation disorder
 - Medical illness: Temporal lobe epilepsy, tumour, trauma, infectious (syphilis, HIV), SLE
 - Drugs: amphetamines, cocaine, cannabis, PCP (Angel dust), alcohol withdrawal, benzo withdrawal, barbiturate withdrawal
- Assessment:
 - Establish rapport: this will be the first encounter of a lifetime of encounters with mental health services. Try to get off to a good start!
 - Domains for assessment: home, employment/study, activities, drugs, sexuality, suicide
 - Assess social situation, and family views and functioning
- Recovery from psychotic illness:
 - 20% - no further episodes
 - 10 – 15 % die: suicide/early death
 - 60 % ongoing, 20% with serious disability

Treatment of Psychosis

- Early intervention improves outcome, reduces disruption/trauma ('collateral damage'), etc. Important given stage of life (adolescence) and the potential problems for subsequent social and occupational development etc
- Treatment programme involving health professionals, family members, support agencies, and cultural/community context
- Brain's ability to process and interpret information is affected ⇒ think carefully about how information conveyed is received. Keeps the facts simple, avoid distractions and pressure, ask one question at a time, give plenty of time to answer
- Biological treatment: treat early, immediately if psychotic, key issue with maintenance medication is compliance
- Psychological: supportive, education, self-care skills. Social skills training and community integration skills → overcome withdrawal → significant ↓ in readmissions
- Social: assertive (to combat stigma), community care
- Relapse prevention: understanding drugs, warning signs, prognosis, side effects

Antipsychotic Medication

- = Neuroleptics or major tranquillisers
- May also use lithium, carbamazepine, antidepressants and benzodiazepines for psychosis
- Reduced risk of relapse in schizophrenia, but 40% will still relapse within a year
- Two effects:
 - Reduces delusions and hallucinations (may take 1 –2 weeks)
 - Tranquillising/calming effect (↓acute agitation, immediate effect)
- For first presentation, treat with low dose and use atypicals (↓side effects → ↑compliance). Use adjunctive long acting benzodiazepine for first few weeks to sedate and ↓agitation
- Can be administered orally, IM, IV and some as depot (but not yet for atypicals)
- Side effects range over sedation, extra-pyramidal, anti-cholinergic and hypotensive
- All relatively effective at reducing positive symptoms, but 'atypicals' better than 'typicals' at reducing negative symptoms (eg ↓motivation, interest, lack of emotional display, restricted speech)

- All have hepatic elimination

Class	Drug	Side Effects			T½	Dose equity
		EPS	Hypotensive	Sedation		
<i>Typicals:</i>						
Phenothiazine	Chlorpromazine	+	+++	+++	16 – 30	100 (ie low potency)
	Thioridazine	+	+++	+++	26 – 36	100
	Trifluoperazine	+++	+	+/-		5
	Fluphenazine *	+++	+	+/-	35	3 (ie high potency)
Butyrophenone	Haloperidol *	+++	+	+/-	10 – 22	3
	Thioxanthenes	Flupenthixol *	++	+	+/-	35
	Thiothixene	++	+	+/-	35	6
						4
<i>Atypicals:</i>						
Azepine	Clozapine	+/-	+++	+++	9 - 17	60
	Olanzapine	+/-	+/-	++	30	3
	Benzisoxazoles	+/-	++	+	2.5	2
* = Available as depot						

Typicals (ie Older antipsychotics)

- Mode of action: block dopamine (D2) receptors. Most also have low affinity for 5HT2 receptors.
Varying amounts of anticholinergic, antihistamine and anti α -1 effects
- Adverse Effects:
 - Extrapyramidal Syndromes (EPS):
 - Acute: Occur early in treatment – usually first two months.
 - Dystonias (muscle cramps and spasms): treat with benztrapine parenterally
 - Akathisia (restlessness): treat with β blocker or benzodiazepine
 - Parkinsonism (tremor, cog wheel rigidity, bradykinesia, mask like face) – may improve with time
 - Anticholinergics only indicated in those whose antipsychotic dose cannot be safely reduced.
(= antiparkinsonian medication, eg antimuscarinic drugs such as Cogentin)
 - Tardive Dyskinesia:
 - Late onset dyskinetic syndrome due to antipsychotic drug treatment. Usually months or years after treatment
 - Fairly common: 15 – 30%
 - Slow, repetitive involuntary movements of mouth/face, and maybe limbs and trunk.
Disappear during sleep
 - Risk factors: old age, organic brain disease, negative symptoms, alcohol abuse
 - Irreversible in 50%
 - No established protocol for treatment: try dose reduction, lithium, or change to clozapine
 - Made worse by dopaminergic agonists and anticholinergics
 - Other effects:
 - Sedation
 - Anticholinergic effects (dry mouth, constipation, blurred vision, urinary hesitancy)
 - α blockade (postural hypotension, tachycardia, delayed ejaculation)
 - Endocrine effects (\uparrow PRL, *marked weight gain*, \downarrow libido, impotence, amenorrhoea)
 - Neuroleptic Malignant Syndrome: Rare (0.2 – 1%) with hyperthermia, rigidity, and impaired consciousness. 20% mortality. Emergency treatment (cooling, fluids, etc)
- Interactions:
 - Potentiate sedation with hypnotics, alcohol, opioid analgesics
 - Fluoxetine increases risk of EPS

Atypicals

- Clozapine:
 - Mode of action: numerous receptors: D1, D2, D4, 5HT2, blocks α -1, H1 and muscarinic receptors

- Effective in individuals not responsive to classical antipsychotics, effective for positive *and* negative symptoms, no extrapyramidal side effects, no impact on sexual or reproductive function.
- Side effects:
 - Sedation, tachycardia, constipation, weight gain, and seizures (3% at highest dose)
 - Agranulocytosis/blood dyscrasias in 1-2 % by 1 year, most in first 18 weeks → regular blood tests
 - Potent enzyme inhibitor: significant drug interaction potential
 - Serotonergic crisis with SSRIs
 - Hypersensitivity syndrome: PUO, arthritis, rash
 - Prolongation of QT
 - Myocarditis
- Risperidone:
 - Mode of action: binds to 5HT2 and D2 receptors, antagonises H and α-1 receptors
 - Similar efficacy as other antipsychotics for positive symptoms. Effective for negative side effects and also affective symptoms (depression, anxiety).
 - Some dose related extrapyramidal side effects. ↑PRL at high doses. Also insomnia, agitation, anxiety, headache
- Olanzapine:
 - Mode of action. Similar to clozapine. Like clozapine has minimal impact on PRL
 - Similar efficacy to haloperidol, but more impact on negative symptoms
 - Sedation, headache, dizziness, constipation, dry mouth, weight gain

Dementia

- = Chronic, generalised impairment of memory (key feature), intellect, and personality with no impairment of consciousness (cf delirium)
- Acquired
- Not a feature of normal ageing
- Diagnostic criteria:
 - Development of multiple cognitive deficits including both:
 - Memory impairment (either ability to learn or recall), and
 - One of aphasia (language disturbance), apraxia (impaired motor co-ordination), agnosia (impaired recognition despite intact sensory function), disturbance in executive functions/personality/social conduct
 - Not due to general medication condition, substance use, or *delirium*
 - Significant impairment in social or occupational functioning, and a decline on previous function
- Epidemiology: 5% of 65 – 80 year olds, 20% of those over 80
- Assessment:
 - General: age, absence of psychiatric history or co-existing physical illness
 - General account from carer, including memory impairment, behaviour change, mood change, physical symptoms, disruption of ADLs
 - Onset: insidious or acute
 - Stepwise deterioration (suggests vascular), seizures
 - Fluctuation, including early evening, nocturnal worsening (“sunsetting”)
 - Family history including Huntington’s
- Clinical Course:
 - Amnesia:
 - Early: forget names, appointments, repetitive in conversation, some insight, leaving elements or taps on
 - Later: forget faces, recent events
 - Advanced: forget past, identity, relatives, no insight
 - Language:
 - Early: difficulty word finding
 - Later: ↓articulateness, difficulty following conversation
 - Advanced: rambling, incoherent
 - Dyspraxia (difficulty sequencing tasks): Difficulties with dressing, cooking → safety issues: wandering, kitchen/road safety
 - Other: depression (difficult to distinguish), psychosis, personality & behavioural change

- Examination:
 - General: posture, gait, consciousness level, wandering, restlessness, feeding and dressing difficulties
 - Mental Status examination
 - Neuro: focal signs, involuntary movements, pseudobulbar signs (swallowing, speech production), primitive reflexes
- Investigation:
 - Cognitive Function: test with mini-mental state: 26 or above = normal, 20 – 26 = mild, 11 – 20 = moderate, < 10 = severe
 - FBC (macrocytosis) and LFTs: is it alcohol induced?
 - Exclude: thyroid, space occupying lesion, B12 deficiency, AIDS, syphilis
 - CT if focal neurological signs, new or odd psychiatric disorder, or age < 75 with shorter history. NB include temporal lobe orientated views, as atrophy of medial temporal lobe is one of the earliest CT findings in Alzheimer's disease
- Treatment:
 - Treatment of any cause found. Treatable causes include:
 - Benign brain tumour, especially subfrontal meningioma
 - Subdural haematoma
 - Wilson's disease: akinetic rigid syndrome, bulbar palsy
 - Deficiency: B12, B6, B1
 - Hypothyroidism
 - Alcoholic dementia
 - Infection: HIV, syphilis
 - Improve functional ability, relieve distressing symptoms (eg secondary incontinence), regular routines (diaries, reminders), establish enduring power of attorney early on (using PPPR act later on is more involved), practical assistance (eg meals on wheels, rest home care), support for the family (involvement in rehabilitations, information, etc)
 - Drugs:
 - Cholinesterase inhibitors:
 - Hold off progression for a year or two? Better motivation, improvement in ADLs
 - 12 weeks before effect can be reliably assessed
 - Side effects: nausea, diarrhoea, vomiting, muscle cramps, fatigue, anorexia
 - Eg Rivastigmine (Exelon): titrate up monthly: 1.5 mg bd → 3.0 mg bd → 4.5 mg bd → bd 6.0 mg
 - Eg Donepezil (Aricept): 5mg od → 10 mg od after a month if necessary
 - Cautions: peptic ulcer disease, arrhythmias
 - Not currently funded and pretty expensive
 - Other drugs with possible benefit:
 - Antioxidants (eg vitamin E)
 - NSAIDs
 - Oestrogen
 - Treatment for vascular dementia: control of blood pressure and aspirin

Aetiology

- Alzheimer's:
 - 50%. F > M. Course 6 – 8 years (⇒ may die of something else first)
 - If < 65 then Alzheimer's disease, if > 65 then Senile dementia, Alzheimer's type
 - Clinical diagnosis. Diagnosis only certain at autopsy
 - Presentation:
 - Marked impairment of memory: anterograde and retrograde (eg how old are you, are you married, what are your children's names, etc)
 - Aphasia with word finding defect early on
 - Visuo-spatial problems: getting lost
 - Loss of interest: hobbies, dealing with finances, new circumstances, etc
 - Gross pathology: Atrophy in frontal, parietal, occipital and temporal regions, with secondary widening of sulci and dilation of ventricles
 - Micro:
 - Neurofibrillary tangles: intracytoplasmic bundles of filaments that displace the neuron's nucleus. Contain abnormal form of the protein tau

- Senile plaques: extracellular intracortical spherical clusters of dilated axons and dendrites surrounding a spherical deposit of amyloid fibrils (amyloid beta peptide). Motor and sensory cortex sparing. A few are normal. There are lots in Alzheimer's
- Amyloid angiopathy
- Granulovacuolar degeneration: clear intraneuronal cytoplasmic vacuoles
- Pathogenesis:
 - ?Accumulation of amyloid beta protein, with failure to exocytose the protein
 - Apoe4 allele is a marker for Alzheimer's but is not yet recognised as a screening or diagnostic tool
- Vascular:
 - 20%. Previous history of CHD, stroke, high BP, etc. M > F
 - Caused by discrete infarcts (ie multi-infarct dementia) but also small vessel disease (eg cerebral arteriolar sclerosis from chronic hypertension)
 - Presentation: Often impaired attention and frontal features, emotional lability
 - Multiple subcortical white matter injury → Binswanger disease (damage to association fibres)
- Diffuse Lewy Body Dementia: 20%:
 - Often associated Parkinsonian features (rigidity, tremor and bradykinesia) – less tremour but trunkal rigidity
 - Can have fluctuating attention and visual hallucinations (so like delirium)
 - Very sensitive to anti-psychotics. A small dose can → profound tranquilliser effect
- Pick's Disease: Much less common, but similarities with Alzheimer's. Differences are early onset of personality, behavioural changes and language impairment. Atrophy of frontal and temporal lobes (ie clearly localised). Microscopically, surviving neurons show ballooning degeneration (Pick's cells) and Pick's bodies (filamentous intracytoplasmic inclusions). No senile plaques or neurofibrillary tangles
- Alcoholic Dementia. See Pathological Effects of Alcohol on the Brain, page 451
- Rarer causes:
 - Creutzfeldt-Jakob Disease (CJD)
 - Fatal, rapidly progressive dementia with psychiatric and behavioural disturbances. Less than 1 per million per year, usually elderly
 - No helpful lab findings (including CSF)
 - Aetiology: abnormal neuronal protein coded by the PRNP gene. Prion causes conformational change from a α -helix to a β -pleated sheet → chain reaction → neuronal death
 - Can be transferred via pituitary extracts, dural grafts, etc
 - 15% of cases familial
 - No macroscopic changes. Microscopically: spongiform encephalopathy – vacuoles in neurons and neuropil (ie extracellular) → neuronal loss and gliosis (marked astrocytosis)
 - Variant CJD (vCJD). Affected young adults, progressed more slowly, early behavioural changes. Spongiform changes plus plaques composed of prion protein. Caught from Bovine Spongiform Encephalopathy (BSE, Mad Cow Disease). Prions very difficult to inactivate (eg standard disinfectants, formalin, UV light don't work)
 - Huntington's Disease:
 - Prevalence: 7 per 100,000
 - Clinical: Choreaathetotic movements and progressive dementia from age 35 – 40. Depression, erratic behaviour, apathy, problems with speech and swallowing. Death in 15 years on average
 - Genetics: Autosomal dominant, short arm of chromosome 4
 - Gross: diffuse gyral atrophy, marked atrophy of caudate nucleus and putamen, dilation of ventricles
 - Micro: loss of neurones in atrophied areas, replaced by fibrillary gliosis
 - HIV & syphilis

Dementia Due to Head Trauma

- = Presence of dementia directly due to head trauma
- Severity and type of cognitive or behavioural impairment depends on location and extent of injury
- Symptoms include aphasia, attention problems, irritability, anxiety, depression, apathy, aggression, other personality change
- Is usually non-progressive unless repeated head trauma (eg boxer). Progressive decline following single trauma suggests another problem (eg hydrocephalus or major depressive episode)

Management

- Fatigue and stress result from:
 - Poor concentration, impaired executive function and ↓memory due to injury
 - Sleep requirements increase, but patients try and do the same amount as before
 - No knowledge about what to expect (both patients and families)
- Fatigue + stress → frustration, anxiety and depression. So reduce factors leading to fatigue and stress
- Management focuses on:
 - Education
 - Proper assessment of cognitive deficits by a psychologist (eg cognitive testing = neuropsychological testing)
 - Support from informed family, friends and employers
 - Regular breaks/sleeps. Take things in small bites and structure day around these
 - Teach relaxation methods
 - Compensating for cognitive losses: structured day (↓ability to plan), lists, diaries
 - Continual reassurance
 - Medication:
 - Use for depression if symptoms do not resolve with counselling and support. SSRIs have least side effects. TCA if headaches, or sleep is a problem (side effects include daytime sedation and ↓cognitive function)
 - Maybe Methylphenidate (Ritalin) - ↑arousal to extend time possible to work

Prognosis

- Only 20 – 30% return to full function 1 – 2 years after a mild head injury
- Degree of cognitive difficulty in first month NOT a good prognostic indicator
- Need to consider PTSD as differential or co-existent diagnosis
- Good prognostic indicators: strong social support, early intervention by a specialist HI recovery service
- Bad prognostic indicators: persisting cognitive difficulties at 6 – 9 months

Delirium

- Global and transient disturbances of consciousness, attention, perception, thinking, memory, psychomotor behaviour, emotion and sleep-wake cycle
- = Acute Confusional State
- Epidemiology:
 - Rare in the community
 - Common in hospital, especially in elderly, 10 – 25% of > 65 years olds admitted to medical wards
 - Significant mortality: approx 25% of elderly patient acquiring delirium in hospital die
- Will get poor history from the patient. Need informant

Symptoms

- Rapid onset (potentially related to new illness/drug). Rarely lasts more than several weeks
- Fluctuating consciousness (cf psychiatric illness, which does not present with impaired consciousness)
- Marked abnormalities of attention and concentration
 - Attention unfocused
 - Thinking: disorganized, delusions, rambling incoherent speech
 - Memory impairment
- Perception: illusions and hallucinations (especially visual)
- Psychomotor behaviour: over/under active, purposeless
- Mood: labile, agitation, fear, anxiety
- Sleep-wake cycle: disrupted or even reversed

Aetiology

- Common causes: Often multi-factorial – a little bit of a number of things
 - Infection: UTI, pneumonia
 - Drug reactions
 - Hypoglycaemia
 - ↓O₂ or ↑CO₂
- Comprehensive list:
 - Drugs: antiarrhythmics, antibiotics, anti-virals, anti-fungals, β-blockers, etc. etc

- Drugs of abuse
- Withdrawal: alcohol, amphetamines, barbiturates, benzos, cocaine
- Neurologic: stroke, epilepsy, Parkinson's, Huntington's, MS, Tumour, normal pressure hydrocephalus (confusion, incontinence, gait disturbance)
- Endocrine: Hyper/hypothyroidism, hyper/hypoPTH, Hyper/hypoadrenocorticism, diabetes mellitus, phaeochromocytoma, etc
- Metabolic: hyponatraemia, hypokalaemia, hyper/hypocalcaemia, acidosis, hypoxia, uraemia, porphyria
- Vitamin deficiencies: thiamine, folate, B12
- Infection: Especially chest and urinary tract, also sepsis, meningitis, encephalitis, AIDS, Hepatitis, etc
- Other: lung/pancreatic cancer, paraneoplastic syndromes, SLE, etc
- Differential of acute confusion:
 - Psych illness: delirium, psychosis, dementia, depression
 - Drugs, illness, metabolic, trauma, hypoxia, poisoning/overdose, post-ictal, ↓thiamine

Risk factors

- Multiple, severe or unstable medical problems
- Dementia or cognitive impairment
- Polypharmacy
- Metabolic disturbances
- Advanced age (especially > 80 years)
- Infection (especially UTI)
- Fractures
- Visual impairment
- Fever or hypothermia
- Psychoactive drug use

Treatment

- First, recognise the delirium (it often isn't). Careful and repeated assessment. Watch for confused/disorientated behaviour or inattention, especially at night
- Examination:
 - Mini-mental
 - Temperature, hydration, ketosis, foetor
 - Signs of injury, including scalp
 - Infection screen
 - Neuro exam
 - Signs of drug abuse
- Investigations:
 - Bloods: FBC, ESR, U&E, Glucose, Ca, Renal, Liver, Thyroid, Thiamine
 - Urine, ECG, CXR
 - Consider: blood alcohol, cardiac enzymes, blood culture, ABG, B12/folate, CT
- Treatment of underlying cause: may require history from care giver
- Management of delirium:
 - Supportive:
 - Reorientation (a smoke and a cup of tea works wonders!)
 - Reassurance
 - Attention to noise and light levels (not too much nor too little)
 - Stimulate during the day: get up and dressed, put on glasses and hearing aid
 - Continuity of staffing
 - Family member (or even an orderly) to sit with patient
 - Familiar objects (eg family photos) in the room
 - Stimulate during the day: get them dressed, false teeth in, glasses on, hearing aid in
 - Attention to nutrition and hydration
 - Target risk factors of cognitive impairment, sleep deprivation, immobility, visual and hearing impairment
 - Drugs: only in addition to the above, and usually to treat those caring for the patient!

- Haloperidol 0.5 mg bd (iv if possible): low dose (eg 0.5 – 1.5 mg), especially in elderly, absolute max 2 – 5 mg prn 1 – 2 hourly. Doesn't have anticholinergic side effects, but may cause restlessness. Maori and Pacific Islanders may be more sensitive so lower dose initially
- Lorazepam (short acting benzo) 0.5 – 2 mg q 15 – 20 min iv/im/sublingual/po

Somatoform Disorders

- = Presence of physical symptoms that suggest a general medical condition but aren't explained by that condition, by substances or medications, or by another mental disorder (eg Panic Disorder)
- Must cause significant distress or impairment in social or occupational functioning
- Difficult to manage: need to check for physical conditions → constant testing → reinforces worry. If find something on tests this validates and reinforces the worry
- Processes contributing to symptoms and motivation for symptom production is *unconscious*. *They don't know it's not real.*
- Cultural, stress, developmental and self-esteem factors may contribute

Disorder	Comment
Somatization Disorder	Polysymptomatic, recurrent and chronic, 5-10% of primary population, often young female, system review profusely positive, key differentials: physical disease, depression
Conversion Disorder	Monosymptomatic, mostly acute, high prevalence, often young females, low education, excellent prognosis unless chronic, key differentials: depression, schizophrenia, neurological diseases
Hypochondriasis	Disease concern or preoccupation, middle to older age, especially if previous physical disease, M = F, may be obsessional, course waxes and wanes, key differentials: depression, physical disease, personality or delusional disorder
Body Dysmorphic Disorder	Obsessive pre-occupation with feelings of ugliness or concern with body defect, rarer, adolescence or young adult, key differentials: delusional disorder, depression, somatization disorder
Pain Disorder	'Simulated' pain syndrome incompatible with known physiology or anatomy, female to male is 2:1, 4 th or 5 th decade, very common in pain populations, key differentials: depression, physical disease, malingering

Somatization

- = Somatic symptoms with no cause found (+/- anxiety/depression)
- Aim of treatment is to reattribute the symptoms to relate them to psychological problems
- Approach to managing in a non-specialise practice setting:
 - Feeling understood:
 - Take full history, including pain during a typical day
 - Watch for emotional clues or links with stressors: "what are you thinking about when it hurts"
 - Ask about social/family factors
 - Explore health beliefs: "What do you think is wrong"
 - Focused exam
 - Change the agenda:
 - Feedback results
 - Acknowledge reality of pain
 - Reframe complaints: set them in the context of life events. "I'm struck by the fact that these pains started shortly after ... and that you've been crying a lot... Do you think there might be a connection"
 - Making the link:
 - Make the link to life events clearer to the patient
 - Use negotiating style: "Do you think that's possible... perhaps..."
 - Projection: "Has anyone else suffered from symptoms like these... Did your mother get headaches – what caused those"? May be easier to see the connection in others

Disorders due to a General Medical Condition

- Psychiatric symptoms occur in a wide range of medical conditions
- Neurological:
 - Degenerative: Parkinson's, Huntington's, Wilson's → depression, dementia, psychosis
 - Epilepsy: 30 – 50 % have psychiatric illness at some stage, can be due to medication

- Brain tumours: especially frontal lobe or limbic system
- Head injury
- Demyelinating disorders: eg MS
- Infectious:
 - Herpes simplex encephalitis → changed personality, psychosis
 - Rabies, syphilis, CJD, Kuru (in PNG)
 - HIV
- Autoimmune: Systemic lupus erythematosus: eventually 50% have psych symptoms
- Endocrine:
 - Hyperthyroid → confusion, anxiety, agitated depression, manic, delusions, with weakness and muscle loss
 - Hypothyroid → if severe then hypomania, depression, hallucinations
 - Hypercalcaemia (due to PTH disorder) → delirium, changed personality, apathy, ↓cognitive function
 - Hypocalcaemia (due to PTH disorder) → delirium, changed personality, eventually tetany
 - Hypoadrenocorticism (Addison's) → apathy, depression
 - Hyperadrenocorticism (Cushing's) → agitated depression
 - Total pituitary failure → hypothyroid and hypoadrenocorticism
- Metabolic:
 - Hepatic encephalopathy → ↓memory, ↓LOC, changed personality
 - Uraemia encephalopathy: renal failure → ↓memory, ↓orientation, ↓LOC
 - Hypoglycaemia: agitation/restlessness
 - Ketoacidosis → easy fatigue
 - Acute intermittent porphyria → ↑porphyrins (components of haemoglobin synthesis): acute colicky abdominal pain, motor polyneuropathy, psychosis, anxiety, insomnia, lability of mood, depression. Barbiturates absolutely contraindicated. 0.2 – 0.5 % psych patients have undiagnosed porphyria
- Nutritional:
 - Niacin deficiency
 - Thiamine deficiency
 - B12 deficiency → neuro degeneration → depression, irritability, moodiness
- Toxins:
 - Mercury: depression, irritability, psychosis, tremour, weakness
 - Lots of others
- Cancers Eg carcinoma of the pancreas
- Medication:
 - Mood disturbances from: stimulants, steroids, L-dopa, etc
 - A previous condition (eg major depressive disorder) can be triggered by medication with the capacity to cause depressive symptoms

Substance Use Disorders

Diagnostic Criteria

- Two types of disorder:
 - Substance *use* disorders: abuse and dependence
 - Substance *induced* disorders: secondary to substance use (eg withdrawal, psychosis, persisting dementia or amnestic disorders, etc). Require evidence of substance use and are not related to pre-existing problems
- Abuse vs. dependence:
 - Abuse implies use is causing job, social, legal or physical problems or impairing function in some way
 - Dependence (a step worse) requires signs of withdrawal and tolerance
- Used to be a definition for 'the addictive personality type': but research has shown no consistent correlation with the proposed criteria

Substance Abuse

- A maladaptive pattern of substance use leading to significant impairment or distress, manifested by **one** (ie fairly low threshold) or more of the following occurring in the same 12 month period:

- Recurrent substance use resulting in a failure to fulfil major role obligations at work, school or home
- Recurrent substance use in which it is physically hazardous (eg driving)
- Recurrent substance-related legal problems (eg arrests for disorderly conduct)
- Continued use despite it causing or exacerbating persistent or recurrent social or interpersonal problems
- Symptoms have never met the criteria for substance dependence for this class of substance

Substance Dependence

- A maladaptive pattern of substance use leading to significant impairment or distress, manifested by **three** or more of the following occurring in the same 12 month period:
 - Tolerance: either ↑ amounts to achieve intoxication or diminished effect with same amount
 - Withdrawal: either characteristic withdrawal syndrome for that substance, or the same or a closely related substance is taken to avoid withdrawal symptoms
 - Substance is taken in larger amounts or over a longer period than was intended
 - There is a persistent desire or unsuccessful efforts to cut down or control use
 - A great deal of time is spent obtaining, using or recovering from its effects
 - Important social, occupational or recreational activities are given up or reduced as a result
 - Use is continued despite knowing that has caused or exacerbated a physical or psychological problem

Epidemiology

- 1986 CHCH Psychiatric Epidemiology Study: Lifetime prevalence rates:

	Overall %	Male %	Female %
Substance use disorder	21	34	9
Alcohol abuse/dependence	19	32	6
Drug abuse/dependence	6	7	4
Affective Disorders	15	10	19
Major Depressive Episode	13	9	16
GAD	31	27	35
Any eating disorder	1	0.2	2

- Adolescents:
 - 5% of 15 year olds meet criteria for alcohol abuse (Fergusson 1994)
 - Cannabis dependence 7% at 18 years, 10% at 21 years. Higher in males
- Co-morbidity or Dual Diagnosis:
 - Epidemiologic Catchment Area (ECA) Study 1990 found the lifetime co-morbidity of substance use disorders by specific diagnoses:

Schizophrenia	47%
Antisocial Personality Disorder	84% (Abuse a diagnostic criteria)
Anxiety Disorders	15%
Panic Disorder	36%
Obsessive Compulsive Disorder	33%
Mood Disorders	32%
Bipolar Disorder	61%

- Those with a mental disorder have twice the risk of an alcohol disorder and 4 times the risk of any other drug disorder
- Those with a lifetime alcohol disorder have twice the risk of another mental disorder (37%) and 6 times the risk of another drug disorder (22%)
- Those with a lifetime other drug disorder have a 4 times risk of another mental disorder (53%) and 7 times the risk of an alcohol disorder (47%)
- Co-morbidity is higher in institutional settings (70- 80%) than in the community
- ⇒ Dual diagnosis is an expectation not an exception

Models of Aetiology of Addiction

- Disease model: emphasises the biological and genetic basis of addition. Loss of control is a central feature
- Self-medication hypothesis: use specific pharmacological effects to self medicate for psychological disturbance and painful affects

- Biopsychosocial model: Multifactorial causality, interaction of genetic predisposition, biological factors, and psychological and sociocultural factors
- Biological model: impact on mesolimbic reward system – extends from the ventral tegmentum to the nucleus accumbens, with projections to areas such as the limbic system and the orbitofrontal cortex

*Factors influencing behaviour**

- Early childhood learning: modelling by parents and significant others
- Current environment: reinforcement or punishment for different practices (especially if immediate)
- Views/knowledge/beliefs about risk: usually over-rate our health and under-rate the risks
- Our resources (usually an excuse)
- Physical environment (work/home)
- Social influences (friends/media)

History Taking

- Attitude of interviewer important: non-judgemental, empathetic, detached, normalising behaviour, start estimates of use at a high level, person can then say ‘no, not that much’ – feels less judgemental
- Often illegal: won’t tell unless good rapport
- Signs of Substance Abuse
 - Changed behaviour
 - Skipping work/school
 - Drug seeking behaviour
 - Money problems
 - Relationship problems
- Questions:
 - Reason for presentation
 - Which drugs
 - Ever intravenous
 - What are the useful effects – why do you continue to use
 - Quantity and frequency, pattern of use (regular or binge)
 - Cost per week
 - Duration of use, age at first use, reason for first use
 - Heaviest use
 - Have you or others ever been concerned about your use
 - Attempts at cutting down and duration of abstinence, what made you start again
 - Problems associated with use, including relationships, job, legal considerations, etc
 - Any withdrawal effects
 - Past treatment and outcome, what was and wasn’t helpful
 - Relationship to psychiatric symptoms. Do they drink when they’re anxious? Have panic attacks followed ↑ drug use, etc
 - If alcohol, ever been in an accident, had a head injury or fracture
- Medical history, psychological history, social situation
- Family History: check psych, suicide and A&D history
- Corroborative interview
- Drug users have high mortality: health consequences, accidents, suicide, high-risk neighbourhoods, etc
- Physical examination: yellow fingers/teeth, injection marks, liver, cardiac murmurs, pregnancy/STD, mental status, signs of intoxication/withdrawal

Investigations

- Alcohol abuse: ethanol level, also LFT (\uparrow GGT) & FBC (macrocytes), nutrition (eg Fe)
- Blood tests for drug levels: benzodiazepines & morphine levels
- Cannabis: creatinine/cannabis ratio over time
- If any intravenous use check for viral serology: Hep B, C, HIV
- Urine tests: useful for tracking abstinence, but not reliably effective as a treatment strategy. Can do a full drug screen (drugs + prescription medications) for \$160. Verification of sample source is important – minimise the risk of substitution (eg giving you someone else’s urine sample).

Drug	Time after which urine screen will be negative
Amphetamine	1 – 2 days
Cannabis	4 – 28 days
Cocaine	1 – 2 days
Diazepam	2 – 4 days (longer with prolonged use)
Heroin	1 – 2 days
LSD	1 – 3 days
MDMA (ecstasy)	2 – 4 days
Methadone	2 – 4 days

Drugs of Abuse

- If therapeutic index is wide, then it's good for addiction: good effect but few side effects
- IV drugs: opiates, speed, and benzodiazepines. Health risks include infection and non-infectious sequelae
- Marijuana
- Ecstasy – amphetamine (party scene)
- Fantasy – GHBA
- Solvents: younger, failing at school, worried parents, neurological impairment
- Tobacco (See Smoking, page 87)

Dependence resulting from various drugs

Drug Class	Physical	Psychological	Tolerance
Alcohol	3	3	2
Sedatives	3	3	2
Benzodiazepines	1	3	1
Opioids	4	4	4
Stimulants	1	3	4
Hallucinogens	-	2	2
Solvents	1	2	3
Nicotine	1	3	3
Cannabis	-	2	1

Cannabis/Marijuana

- Psycho active ingredient is Δ9 tetrahydrocannabinol (Δ9 THC)
- Receptor targets in the CNS = CB1, in PNS = CB2
- Synthetic cannabinoid drugs used therapeutically for appetite stimulation (eg in cancer), anticonvulsant/antispastic, analgesic
- Effects:
 - Minimal for occasional use, greater for longer-term heavy use
 - Respiratory system: hot irritating smoke → all the effects of cigarette smoke (inflammation, ↑mucus, thickened basement membrane, squamous cell metaplasia, destruction of cilia)
 - CNS: enhanced feelings of well being, disputed dose-dependent effects – reduction in energy, drive and motivation, psychosis, ↓learning and attention, dependence with associated social and psychological dysfunction, acute adverse reactions (eg anxiety/panic attacks)

Regulation of Addictive Drugs

- See Regulation of Drugs of Abuse, page 536

Treatment of Substance Abuse

Treatment Rationale

- Treatment must be for underlying addictive disorder, not just detoxification and withdrawal
- Addiction is a chronic not acute illness. Requires long term follow-up and behaviour modification (as with diabetes and hypertension)
- Often unsympathetic response because addiction is perceived as self-afflicted: but there are numerous involuntary components in the addictive process. Loss of voluntary control turns a drug misuser into drug addicted. There is a compulsive, often overwhelming, involuntary component
- Involves genetic, biological, behavioural and environmental components

- Success rate for treatment depends on type of drug and variables inherent in the population being treated (e.g. better for professionals than for poorly educated). Nicotine has the poorest success rate. Success rates are comparable with other chronic diseases
- Treatment is cost-effective

Issues In Treatment

- Compliance with treatment. Those who comply with treatment have best prognosis – as with other chronic diseases
- Who should be involved: multidisciplinary approach
- Managing the environment: peer pressure, money, job, supports, triggers to former behaviour, family relationships (can they be helped, education about illness)
- The most significant predictor of treatment success is an empathic, hopeful, continuous treatment relationship
- Must also treat any co-morbid diagnosis simultaneously

Types of Treatment

- Medication: Antabuse, naltrexone, opioid substitution
- Detoxification (inpatient/outpatient)
- A&D counselling: motivational interviewing, strategies for change, relapse prevention
- Psychotherapy: CBT, psycho-education
- Self-help groups
- Addressing specific issues: grief, anxiety, childhood sexual abuse, sexual assault, anger, relationship problems, parenting issues, financial, housing, employment issues, etc

Readiness to Change/Motivational Interviewing

- See Behavioural Change, page 11

Services for dependency

- Detox: Kenepuru (inpatient)
- AA
- Narcotics anonymous
- Queen Mary – Hamner: uses 12 step process
- Odyssey House (Auckland)
- Alcohol and drug service

Making the change

- Takes a long time
- Involves changing lifestyles, supports, habits
- GP can assist with motivation for change:

Methadone Treatment

- For opiate addiction
- Methadone is highly addictive, but is regular, long acting (a dose a day holds for 24 – 46 hours), free ($\rightarrow \downarrow$ crime), legal, more effective taken orally than other opiates, no risks from injection
- Doesn't give a high – just stops 'hanging out' (withdrawal)
- Has to be taken every day
- Can cause high mood, drowsiness, \downarrow pain, small pupils, constipation, histamine release (sweating, itching, etc), \downarrow saliva \rightarrow \uparrow tooth decay, \downarrow libido – it is a powerful drug
- It doesn't affect senses, or damage body organs, shouldn't affect pregnancy or breast-feeding
- Is dangerous in conjunction with tranquillisers and/or alcohol \rightarrow overdose situation (eg vomit and choke while sedated)
- Is taken as part of a planned programme, including counselling, to build a life away from opiate abuse – can concentrate on sorting out debt, relationships, etc

Alcohol Abuse

Safe Limits and Metabolism

- Men and women have different blood alcohol levels given the same dose due to lower Vd in women

	Standard Units	One Sitting	Per Week
Male		4, with 2 – 3 alcohol free days a week	14 – 21 (ie up to 210 g ethanol)
Female		3, with 2 – 3 alcohol free days a week	7 – 14 (ie up to 140 g ethanol)

- Standard Unit = 10 g of alcohol. E.g. 1 can normal strength beer, 1 glass (120 ml) table wine, 1 glass sherry/port, 20 ml spirits (hotel nip)

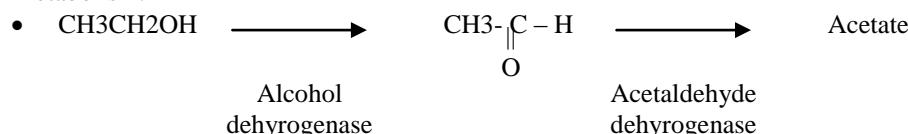
- Effects (if no tolerance):

- 50 mg: relaxation, emotional liability
- 100 mg: judgement affected, reactions slow
- 150 mg: amnestic blackouts (can't remember afterwards)
- 200 mg: ataxia, vomiting, nystagmus, drowsiness
- 350 mg: coma, respiratory depression, death
- Intoxication can be life threatening

- Driving:

- Legal blood limit = 80 mg/100ml (17.4 mmol/L)
- Legal breath limit = 400 µg/L breath
- Driving skills impaired from 40 – 50 mg/100 ml

- Metabolism:



- 10 g per hour, zero order kinetics
- = 15 – 20 mg/100 ml blood/hour (3 – 4 mmol/hr) = one standard drink
- Twice this rate of clearance with chronic alcohol consumption, less in liver disease
- Alcohol changes NAD/NADH ratio → alters redox potential → widespread effects (eg ↑ lipids, ↓ sugars, etc)

Classifying alcohol use

- Alcohol Dependence:** need to drink every day
 - Important features:
 - Tolerance: due to pharmacodynamic and pharmacokinetic (eg enzyme induction) processes
 - Cross-tolerance, eg alcohol and BZDs
 - Physical dependence: Withdrawal syndrome on abstinence
 - Psychological dependence: Emotional need to compulsively take a drug (even if no physical withdrawal syndrome)
 - Characterised by: ↑tolerance (CNS adaptation and pharmacokinetic), narrowing of drinking pattern (stereotyped drinking), amnesic blackouts, withdrawal symptoms, awareness of loss of control, failed attempts at abstinence, preoccupation with drinking, drinking to relieve withdrawal symptoms
 - Look for: compulsive binges with ↑ frequency, stereotyped drinking, intake over 60 g ethanol/day, chronic social and health problems, neurological problems
 - Use CAGE questions to assess dependency: Have you ever tried to Cut Down, Annoyed by others telling you to cut down, Guilt, Eye-opener
- Hazardous Drinking.** Heavy drinking with no “obvious” problem
 - Characterised by prolonged (eg 5 years or more), regular (eg almost daily, or weekend binges), excessive consumption with a high risk of physical mental and social implications, but no dependency features – but maybe some ↑tolerance and occasional amnesic blackouts, may not be associated with acute intoxication
 - Look for: episodic heavy social drinking to intoxication, increasing psychosocial problems, accidents, inflammation of stomach, liver, pancreas

- **Problem Drinking:** problems related to alcohol without dependency and with or without excessive regular consumption. May result from isolated acute intoxication or drinking with medical contraindication – injury, aggression, binge drinking, family, financial, occupational problems
- Remember: Drug abusers often abuse multiple drugs (eg alcohol, BZDs, and marijuana)

Assessment

- For liver and pancreatic effects see Alcoholic Liver Disease, page 185
- Differential of drowsiness/confusion in alcoholic:
 - Alcohol intoxication
 - Sedatives
 - Post-ictal (eg seizures with alcohol withdrawal)
 - Wernicke's encephalopathy
 - Subdural haematoma: grow slowly, compounded by global atrophy due to alcohol
 - Hepatic encephalopathy
 - Alcoholic hypoglycaemia
- Assessment of co-existing disease is vital:
 - Other drug use (BZD, sedatives, opioids → also have withdrawal features)
 - Primary depressive disorder (in addition to alcohol-induced depression which resolves quickly)
 - Gastro disorders: oesophagitis, pancreatitis, liver disease, small bowel dysmotility
 - Respiratory: Obstructive sleep apnoea, aspiration pneumonia, TB
 - Musculoskeletal: chronic proximal myopathy, osteoporosis
 - Carcinomas: larynx, oesophagus, lung
 - Neurological: peripheral neuropathy, dementia, cerebellar atrophy, Wernicke-Korsakoff syndromes, Head injury (subdural haematoma), haemorrhagic stroke
 - Cardiovascular: arrhythmias, congestive cardiomyopathy, hypertension
 - Blood and nutritional: macrocytosis, folate and iron deficiency, impaired leucocytes, hypocalcaemia, hypokalaemia, electrolyte disturbances
- Investigations:
 - Alcohol levels
 - LFT
 - FBC (anaemia)
 - Glucose (→ ?hypoglycaemic)
 - Coagulopathy: INR
 - Other drugs, eg BZD

Pathological Effects of Alcohol on the Brain

- Cerebral atrophy:
 - Common. Seen in over ¼ of long term alcoholics at post-mortem
 - Ventricular dilation, widening of the cerebral and cerebellar sulci
 - No specific cortical changes have been described. No classical changes of multi-infarct dementia or Alzheimer's (see Dementia, page 439)
- Wernicke-Korsakoff Syndrome:
 - Due to ↓**Vitamin B1** (Thiamine) – Marmite and Cereals are good sources
 - Thiamine is not stored in the body, signs of deficiency can appear within a month – especially in beer drinkers (high carbohydrate intake →↑ thiamine requirement)
 - Rare triad of:
 - VI nerve palsy (→vertical/horizontal nystagmus)
 - Ataxia (vestibular dysfunction)
 - Confusion
 - Pathology:
 - Acute: petechial haemorrhages in the grey matter surrounding the third and fourth ventricles and aqueduct
 - Chronic: shrinkage and haemosiderin staining (especially of mamillary bodies)
 - If prolonged leads to Korsakoff's amnesic psychosis
- Vitamin B12 (cobalamin) deficiency:
 - Leads to:
 - Peripheral neuropathy, demyelination and degeneration of the posterior and lateral columns of the spinal cord
 - Variety of confusional, amnestic and psychotic alterations

Treatment of alcohol abuse

- Drug treatment of alcohol abuse:
 - Effects of chronic alcohol:
 - ↑Dopamine activity
 - ↑Opioid activity (\Rightarrow ?naloxone/naltrexone \rightarrow ↓craving)
 - ↑Sensitivity to GABA
 - ↓Serotonin activity
 - Ie, lots of potential neurotransmitter targets in reward pathways to ↓cravings, etc
 - Antabuse (disulphiram):
 - Blocks second step of metabolism pathway \rightarrow ↑acetaldehyde \rightarrow flush, vomiting, ↓BP
 - Takes 12 hours to block enzyme system. Has effect within ½ hour of a drink (one drink is enough)
 - Contraindications: heart disease (can't cope with ↓BP), makes depression/psychosis worse
 - Administration needs to be supervised: if taken at own discretion then little impact on abstinence
 - Acamprosate (Campral): ↓craving, must be taken 3 times daily (a pain!), start 7 days post detox. Not in elderly, pregnant, liver or renal disease. No hypnotic, anxiolytic or antidepressant effects
- For non-drug treatment, see Treatment of Substance Abuse, page 448

Alcohol Withdrawal

- Most common drug withdrawal state. Can be life threatening (unlike opioid withdrawal)
- Detoxification is only the first step in treatment
- Aetiology of alcohol withdrawal syndrome poorly understood
- Features of withdrawal:
 - A spectrum. Delirium Tremens describes severe withdrawal only
 - Minor withdrawal (peaks at day 2): restlessness, anxiety, nausea, disordered sleep, headache, tachycardia, hypertension, tremor
 - Major withdrawal (peaks at day 5): Agitation, behavioural disorders, confusion, sweating, fever, paranoia, hyperventilation
 - Seizures: if they occur, are most likely on day 1 – 3, usually only one, usually grand mal, status rare
 - Hallucinations: usually visual (auditory unlikely), on day 2 – 4
- Management:
 - Get pre-detoxification blood alcohol level. Helps with assessment (how tolerant are they?). Avoid too much sedative if high. Alcohol metabolised at 20 mg/dl/hour (4 mmol/L/hour) – can predict when it will reach zero
 - Previous withdrawal severity good indicator of likely current severity. Other indicators of severity: > 15 standard drinks a day, early morning drinking, hypokalaemia, intercurrent illness
 - If likely to be severe, or if co-existing medical, psychiatric illness or other addiction, withdrawal should be medically supervised (ie admit them). Mattress on the floor with constant nursing attention. If dehydration or constant sweating then iv fluids
 - Otherwise at home or outpatients if good social support
 - Routine blood tests: FBC, ESR, U+E, B12/folate, LFT, AST, GGT, PT, BS
 - Parental thiamine followed by short oral course (25 mg po twice daily)
 - Treat withdrawal with drugs which have cross-tolerance with alcohol (ie BDZs) *once they're no longer intoxicated*
 - Use BDZs or chlormethiazole
 - Give sedatives with extreme caution if measurable blood alcohol levels
 - Diazepam 10 – 20 mg/4 hourly for moderate withdrawal, 20 mg/2 hourly iv for severe. Resist protracted sedatives, otherwise \rightarrow addiction. If liver disease then reduce dose
 - Oral chlormethiazole 1 gm 6 hourly
 - Additional treatments:
 - β blockers for tremor, hypertension (except if CORD or CV disease).
 - Haloperidol 1 – 5 mg 6 hourly if hallucinations
 - Sodium Valproate (Epilim) 600 mg stat po, then 400 mg 8 hourly for 5 days, if history of seizures – care if liver disease. Likely to occur early in withdrawal, especially if history of seizures with previous withdrawal

Other Disorders

Eating Disorders

History Questions

- Do you worry about how much you weigh?
- What do you think of your body/weight?
- Do you diet?
- Do you ever make yourself sick after a meal?

Anorexia Nervosa

- Low weight not due to other illness
- Persistent refusal to maintain weight (cf depression – don't want to eat). Obsession with food, weight and thinness
- 90% female, usual onset from 11 – 19 years
- Aetiology:
 - Media message: thin = beautiful
 - Already painfully aware of body image due to changes in puberty
 - Stressful life situations
 - Genetics
 - Family dynamics
 - Something they can have control over when they don't have control in other areas of their lives
 - Failure to achieve weight control → ↓sense of failure → try harder
- Signs:
 - Deliberate self-starvation
 - Fear of gaining weight
 - Denial of hunger
 - Constant exercising
 - Self perception of being fat
 - Absent or irregular periods
 - May purge (vomiting, laxatives)
- Complications: starvation, heart, osteomalacia, ↓fertility

Bulimia

- Purging a more dominant feature
- Don't usually loose so much weight

Impulse Control Disorders

Gambling

- Reference: General Practitioners Manual on Problem Gambling, Compulsive Gambling Society of NZ
- = The addiction you can't see. The new mental disorder on the block
- Epidemiology:
 - 1 – 3 % of population are pathological gamblers. There are no longer stereotypical groups – young and women also now affected
 - Maori 3 times more likely, Pacific Islanders 6 times more likely (heavy socio-economic confounding)
 - 2/3 of presenting problem gamblers are under 30. Average age is decreasing
 - 90% of the population gamble (Dept Internal Affairs figures). \$600 per family per year (cf \$200 in the US)
 - Gambling has increased by 700% in the last decade. There has been significantly increased access to all forms of gambling (without social research)
 - Mode of gambling of people with pathological gambling disorder: 60% non-casino pokies
- Diagnosis:
 - Should screen early on in relationship with GP: later on won't tell due to embarrassment
 - Features: Preoccupation with gambling, needs to gamble more to get the same excitement (ie tolerance), repeated and unsuccessful efforts to cut back or control, restless or irritable when trying to cut down (ie withdrawal), gambles as a way of dissociation, after loosing returns to chase their losses, lies to conceal extent of gambling, has jeopardised or lost a job or relationships, etc

- Other features:
 - Impacts for physical health: can't afford to go to doctor, usually heavy smokers, often have co-morbid anxiety, depression, alcohol or drug disorder (NB – screen for depression in affected families), high suicidality
 - Will use their own money then may resort to crime (usually fraud, forgery & theft). Crimes unsophisticated, effected in haste and often first offence
- Theories re aetiology:
 - Reward deficiency syndrome
 - General theory of addiction: unresolved/maladaptive issues from the past
 - Behavioural/environmental conditioning
 - Social learning (eg permissive culture)
- Phases in the course of the illness:
 - For gambler: winning, losing, desperation, critical, rebuilding, growth
 - For spouse: denial, stress, exhaustion, critical, rebuilding, growing
- Problems with thinking in gamblers:
 - Irrational style of thinking
 - Illusions of control ("if I study the horses enough I'll win")
 - Superstitious beliefs ("I feel lucky today")
 - Biased evaluations
 - By the time gambling is pathological, they don't care whether they win or lose, just want to do it
- Help to offer:
 - Treat depression
 - Financial/budget advice: easy way to engage, encourage contemplation
 - Information (eg about 'controlled gambling' as an option for 'early' problem gamblers)
 - Helpline: 0800 NOGAMBLE
 - Referral services: outpatients, Compulsive Gambling Society, Odyssey House

Fictitious Disorder

Factitious Disorder by Proxy

- = Munchausen's By Proxy
- Criteria:
 - Intentional production or feigning of physical or psychological signs or symptoms in another person under the individual's care
 - Motivation is to assume the sick role by proxy
 - No external incentives for the behaviour (economic gain, avoiding legal responsibility)
- Warning signs: child aged 15 months to 6 years, baffling multisystem symptoms, taken to lots of health care providers, over attached parent, no symptoms when parent absent, strange poisonings, reported seizures

Personality Disorders

Diagnosis

- Personality disorder =
 - An enduring pattern of inner experience and behaviour that deviates markedly from the expectations of the individual's culture
 - Is inflexible and pervasive across a broad range of situations
 - Has its onset in adolescence or early adulthood, is stable over time and leads to distress
 - And is manifested in two or more of the following: interpersonal functioning, affectivity (emotionality), impulse control, cognition (style of thinking)
- Key characteristics:
 - Rigidity: very pervasive rigidity of cognitions and behaviours
 - Avoidance: don't want to look at or experience their thoughts or feelings → problem for therapy (compulsory treatment won't change anything)
 - Long-term interpersonal difficulties
- Differentiating from axis 1:
 - There is substantial comorbidity with axis 1 – but must be distinguished from axis 1 (which is episodic, different from normal state. Personality disorders ARE the normal state)

- Need to exclude other possible factors: eg substance abuse, head injury, general medical condition, mood or psychotic disorder (ie must not occur exclusively in the course of an axis 1 disorder)
- Consider axis 2 if: ongoing non-compliance, client unaware of effect of their behaviour on others, client acknowledges need for change but motivation is questionable, always blame others for their behaviour
- Can't diagnose before age 19 (much of the description of the disorders is also descriptive of adolescence)
- Requires longitudinal assessment and collateral information
- Must evaluate within a cultural and religious context (DSM 4 is white & American)
- Labelling someone with a personality disorder can be difficult, given limited information and possible reactions → often people labelled 'traits of disorder X'
- Presentation is often not for the disorder (as it could be, for example, for depression), but for the degree of impairment due to excessive or little compliance with treatment
- Treatment is difficult and long-term: given deeply imbedded nature and genetic predisposition to personality
- Explanation to client:
 - Behaviours were probably adaptive to survive difficult childhood experiences (at some point behaviours were helpful – but they've got stuck). Take care to look for an explanation not someone to blame (people usually do the best they can)
 - But it is now more functional to use different strategies in different situations
 - Take care of criticising non-compliance: few are proud of 'doing what they're told' – would you rather be a sheep or an eagle?

Examples of Personality Disorders

Disorder	Comment
Cluster A: Appear odd or eccentric	
Paranoid	Generally distrustful, suspicious, loners. Non-compliant with treatment as it doesn't fit their worldview. See less of them in GP – don't call attention to themselves.
Schizoid	Distrust and suspiciousness such that other's motives are interpreted as malevolent
Schizotypal	Detachment from social relationships and restricted range of emotional responses (eg can't express anger, seem directionless)
Cluster B: Dramatic, emotional, erratic	
Antisocial	Acute discomfort in close relationships, cognitive or perceptual distortions, eccentricities of behaviour. Often have ideas of reference (but not with delusional conviction) eg preoccupied with paranormal phenomena or have special powers. Important differential to psychosis. May be suspicious/paranoid, may seek treatment for associated depression or anxiety.
Borderline	Call attention to themselves, vocal in asking for help, other people want them to change but they may see their behaviour as functional (will bear the cost of dysfunction because they get what they want)
Histrionic	Disregard for, and violation of, the rights of others (usually male)
Narcissistic	Instability in interpersonal relationships, self-image, and affects, and marked impulsivity (usually female)
Cluster C: Anxious and fearful	
Avoidant	Excessive emotionality and attention seeking
Dependent	Exaggerated sense of self worth – pattern of grandiosity, need for admiration, and lack of empathy
Obsessive-Compulsive	May come to attention due to anxiety
Disorder Not otherwise specified	Social inhibition, feelings of inadequacy, hypersensitivity to negative evaluation
	Submissive and clinging behaviour, related to an excessive need to be taken care of
	Pattern of preoccupation with orderliness, perfectionism and control
	Meet criteria for a personality disorder, but are a mixture of the above or don't fit any of the above (eg passive-aggressive)

Borderline Personality Disorder

- Incidence: 3 – 5 % (cf 1% for Schizoid)
- Criteria include:
 - Frantic efforts to avoid real or imagined abandonment
 - Unstable and intense relationships alternating between extremes of idealization and devaluation
 - Impulsivity in areas that are potentially self-damaging: eg spending, sex, substance abuse, binge eating
 - Recurrent suicidal behaviour, parasuicides, threats or self-mutilations
 - Marked reactivity or mood, difficulty controlling anger
- Characterised by:
 - Schema: I can't control myself → overdeveloped emotional responsiveness & underdeveloped self-identity, impulse control
 - Core belief about self: I'm defective, helpless, vulnerable, bad
 - Belief about others: other people will abandon me, can't be trusted
 - Combination of these two leads to extremes of behaviour: need to depend on others but will be abandoned
 - Hate being alone: may attend A & E or ring friends late at night for company
- Self-harm:
 - Begins between 10 and 16: often following a major life change
 - 'Toxic self-soothing': eases the inner pain – powerful way to feel better. Can either help the dissociation (turn off emotions) or help them feel real
 - Communication strategy: there is chaos within family and have never asked for help → can't ask for help now. But self-harm is not always a cry for help. For most, self-harm is a private matter
 - Strategy in the game of life: to manipulate people or drive them away
 - Always need to screen for concurrent depressive episode: this will need treatment
- What helps in situations of self-harm
 - Non-judgemental acceptance
 - Teach other ways to self-sooth
 - Deal with trigger event: what causes the negative feelings
 - Address underlying issues: but shouldn't do trauma counselling without also improving coping skills
- Aetiology:
 - Genetic loading in temperament: ↓perseverance, ↑impulsivity, ↓affect regulation, ↑stimulation seeking
 - Sexual abuse in 75% (but not all severely abused develop the disorder): feeling unsafe, victimisation, trauma, terror
 - 75% are female (men more likely to react by becoming antisocial – same motivation but take it out on others rather than themselves – or substance use). Behaviour in collusion with dominant western values (eg emotionality, dependence)
 - Other societal factors eg invalidating environments (eg neglect), marginalisation
 - Most affected people have this cluster of factors, but someone can still get it even if the best of upbringings ⇒ ?stronger than normal predisposing temperaments

Treatment of Mental Illness

Care for the Mentally Ill

- Illness (especially initially) is very traumatic for individual and family (eg may not cope as normal or remember anything you say)
- Families will often blame themselves or feel guilty
- Knowledge/education is key: without it people are powerless
- 'Recovery': issue may not be getting rid of all the symptoms, but getting rid of or managing those symptoms which are disruptive or distressing

Stigma

- Feeling created by stigma is a significant reason for the loss of hope and relapse experience by those with mental illness

- Stigma leads to discrimination and sense of shame
- Common misconceptions:
 - People with mental illness are dangerous and violent
 - People with mental illness never recover: vast majority do recover, some require ongoing treatment
 - It's got nothing to do with me: but mental illness affects people of all ages and backgrounds

Drug Treatment

- When using medication:
 - Don't make assumptions about what people want – ask them
 - What have they used before and what has worked. What's worked for family members?
 - Need to consider side effects: will benefits outweigh costs. Side effects are often significant, and will be a major cause of problems with compliance. Be ready to change medications if side effects are intolerable
 - Need to consider the long term (ie when/how will they come off) as well as the short-term
 - Make sure alternative/adjunct treatments are considered
 - Optimal initial dose: the level at which there are maximum therapeutic benefits for minimum side effects
 - Maintenance dose: lowest possible dose that provides relief/remission. Will vary from person to person, and due to psychosocial factors (ie may need to increase it under when under stress)
 - Regular review is important, until the patient is stabilized on the medication
- Drug education:
 - Understanding the medication's purpose is vital to informed consent and to adherence to treatment
 - Patient needs to know why the medication is needed, what the medication is expected to achieve, when and how to take it, and possible side effects or restrictions (eg diet), the likely duration of treatment, how long until an effect should be noticed, whether the medication is addictive, what are the alternatives
 - Some medication (eg fat soluble anti-psychotics) clears very slowly from the body, so a patient can stop taking them without immediate relapse. Patient's need to understand that the drugs are effective only if taken regularly

Cognitive Behavioural Therapy (CBT)

- See also Treatment of Major Depressive Disorder, page 429
- Was developed as a structured, problem-orientated psychotherapy by Aaron Beck in the 1960s
- Focuses on cognitive and behavioural influences on human experience, as well as interpersonal processes and 'unconscious' motivation/underlying schema
- Draws on my aspects of learning theory and cognitive psychology
- Process in depression: early experience → formation of dysfunctional assumptions → critical incident → assumptions activated → negative automatic thoughts → behavioural, motivational, affective, cognitive and somatic symptoms of depression
- Cognitive triad in depression: negative view of self, of the world, and of the future
- Basic principals of CBT:
 - The situation itself does not determine how people feel
 - Emotions and behaviours are influenced by how people perceive events
 - Information processing biases lead to, or maintain, depressed affect and behaviour
- Efficacy of CBT well supported. At least as effective as antidepressants in depressed outpatients

Problem Solving Therapy

- For 'problems of living' causing or contributing to current symptoms
- Regaining control → ↑mood and less overwhelmed
- 3 Steps:
 - Realise symptoms are linked to problems in their life
 - Define and clarify problems
 - Solve problems in a structured way
- Stages:
 - Explanation of treatment and it's rationale
 - Recognition of emotional symptoms
 - Recognition of problems: eg relationships, work, money, housing, legal, alcohol, etc
 - Acceptance of a link between symptoms and problems
 - Clarification and definition of problems:

- List problems in a concrete form
- Break down big problems into more manageable parts
- Choose achievable goals given patients resources and obstacles
- Patient generates as many solutions as possible
- Choose the preferred solution
- Implement the preferred solution – set deadlines, etc
- Evaluation and encouragement. If unsuccessful consider: low motivation, inappropriate goals, unsuitable choice of solution, inappropriate implementation

Compulsory Treatment

- See also Protection of Personal and Property Rights Act (1988), page 713. Used for people with diminished competence – especially dementia.
- Features of the Mental Health (Compulsory Assessment and Treatment) Act 1992:
 - Specific legal definition of mental disorder (not a diagnostic definition)
 - Even if committed, must be treated in the least restrictive environment (→ community orders)
 - Rights of patients are listed: eg to information, to respect for culture, to second opinion, to legal advice, ability to communicate (phone, letters, visitors, etc)
 - Can't treat without consent (which you must try and get) without a second opinion
 - Review procedures are specified, including the Mental Health Review Tribunal
- Definition of Mental Disorder (Section 2):
 - An abnormal state of mind characterised by continuous or intermittent delusions, disorders of mood, volition (energy, drive, will), cognition, or perception, etc
 - And to such a degree that it poses a serious danger to person or others, or seriously ↓ ability to take care of themselves
 - Exclusions include (Section 4): if due only to intellectual disability or substance abuse, criminal behaviour, sexual preferences, political and religious views
- Process:
 - Application must be made by anyone over 18 (section 8)
 - Medical certificate must be provided by any doctor (who may be the applicant, section 8)
 - Reviewed by a psychiatrist designated under the Act within 24 hours (section 9)
 - 5 day compulsory assessment period (although can be released, become voluntary, appeal, section 11)
 - Following reassessment can be held for a further 14 days (section 13)
 - To extend beyond this require review by family court
 - Compulsory treatment orders:
 - Community treatment orders (section 29)
 - Inpatient orders (section 30)
 - Duly Authorised Officer = usually an experienced CPN in CATT team – carry out assessments, start process

Grief and Bereavement

- Reference: Material from Mary Potter Hospice, obtained in GP run, and Te Omanga Hospice Material
- See also Palliative Care, page 473

Theories of Grief

- Freud: work of mourning: detachment from person who has died. Healthy resolution when this is completed
- Kubler-Ross: Stages of terminal illness: denial, anger, bargaining, depression, and acceptance. But it's not sequential, and this only talks of emotions, not physical or behavioural dimensions
- Worden: Tasks of mourning:
 - Accept reality of loss (harder if no body etc)
 - Experience pain of grief
 - Adjust to an environment in which the deceased is missing (often very practical – change in roles etc)
 - Withdraw emotionally and invest in new relationships (later he revised this to emotionally relocate the deceased and move on) – put the deceased in another place
- Silverman:
 - There is a continuing bond between deceased and survivor

- Stages:
 - Impact: this is not real
 - Recoil: I'm going crazy, why am I worse now (can be months later)
 - Accommodation: what do I carry with me? Being a living memorial – don't have to cut off – can move on and still carry something with them
- Stroebe et al: Dual process moving between expression of grief and containment of grief (women prefer former, men latter)

Characteristics of Grief

- Reassure bereaved person that these are normal. If overwhelming, seek help
- Emotional: bewildering and intense range of emotions without warning - shock, numbness, relief, anxiety, anger, blame, guilt, loneliness, helplessness, hopelessness
- Physical: hollow stomach, tight chest, breathlessness, weakness, lack of energy, ↓sexual desire, sleep disturbances, symptoms similar to person who died (this can be pathological)
- Cognitive responses: disbelief, confusion, ↓concentration, going crazy, preoccupation
- Behaviours: searching, crying, sighing, absent minded, restless, ↓socialising, visiting/avoiding places that are reminders

Coping with Loss

- Losses are a common cause of illness – they often go unrecognised
- Conflicting urges lead to a variety of expression of grief – but there is a pattern
- Understanding factors that predict problems in bereavement enables these to be anticipated and prevented
- Grief can be avoided or it may be exaggerated and prolonged
- Doctors can help to prepare people for the losses that are to come
- People may need permission and encouragement to grieve and to stop grieving

Factors Complicating Grief – Risk Factors for Pathological Grief

- Dependent family members (children, handicapped, elderly)
- Loss of primary care giver/constant companion
- Loss of financial provision
- Loss of home (feared or actual)
- Anxiety about decisions
- Unable to share feelings
- Family discord
- Uncontrolled pain/emotional distress before death
- Concurrent life crisis
- Prolonged reaction/suicidal thoughts
- Lack of community support

Children's Grief

- It is not possible not to communicate to children (ie not telling them is not an option)
- Help should start at the time of diagnosis
- Talk about what won't change as a result of the illness
- Maintain things that are important in a child's life (e.g. routines)
- Talk about practical concerns
- Provide extra stability, order, routine and physical affection
- They need to know who will take care of them if key people leave or die
- Offer reassurance
- Children often assume responsibility for what has happened and feel very guilty
- Offer clear, simple, truthful information: repeat, repeat, repeat
- Don't use euphemisms (e.g. asleep – explain death, body stops working)

Signals for attention from a grieving child

- Marked change in behaviour: illegal behaviour, persistent aggression (> 6 months), tantrums, withdrawal, drug abuse
- Inability to cope with problems and daily activities
- Many complaints of physical ailments
- Persistent depressions, panic attacks

- Change in school performance
- Fearfulness for self, or for loved ones

Helping Families

- Listen effectively
- Foster communication
- Engage siblings
- Check social supports
- Address symptoms
- Provide constant factual data
- Help build positive memories
- Don't take offence

5th Year Written Exam Model Answer

- These questions normally give a small vignette and then ask the following questions

What is the Diagnosis?

- List the factors from the vignette which support your diagnosis
- List what other factors you would ask about on further history taking (eg what criteria for your diagnosis were not mentioned in the vignette)
- What risk factors for the diagnosis are there in the vignette or that you would ask about
- Is there a significant impairment in social and occupational functioning
- Is there a change from previous functioning

What are the possible Differentials?

- Always consider including the following
 - Alcohol and Drug use disorders or withdrawal
 - Other psychiatric disorders (eg anxiety for depression, etc)
 - Conversion disorder
 - Axis 2 disorders (personality disorders)
 - Medical conditions:
 - Endocrine: thyroid, cortisol, calcium
 - Cerebral insult: dementia, stroke, tumour, SLE, AIDS
 - Medications: β-blockers, steroids, etc

What is your recommended management?

- Establish a positive therapeutic relationship based on a shared understanding of the problems
- Establish an accurate diagnosis:
 - Take a full history (including past psych history) and mental state exam
 - Get a corroborative history if necessary
 - Consider a drug screen if indicated
 - Do a physical exam and investigations to exclude medical causes
 - Assess for comorbid psych illness (especially alcohol and drug use)
- Establish a formulation:
 - Why has this person presented in this way at this time
 - Assess predisposing, precipitating, perpetuating and protective factors across a biopsychosocial framework, eg genetic factors, coping and relationship skills, stress, risk factors
 - Consider cultural aspects. Assess their needs and treatment within their cultural context
 - Assess insight, willingness to change or accept help
 - Assess severity
- Immediate management:
 - Safety issues: Use of CAT team, Mental Health Act, etc
 - Do they need admission to stabilise and assess/observe?
 - Immediate drugs for psychosis: antipsychotic +/- lorazepam
- Longer term management:
 - Multidisciplinary approach
 - Lifestyle modification: stress management, ↓alcohol and drug, sleep hygiene, exercise
 - Maintain function and integration with communities of interest

- Education for patient and their family
- Drugs:
 - Side effects, contraindications, duration
 - Watch for and treat complications
- Psychotherapy:
 - Modify exacerbating or precipitating behaviours
 - CBT, coping skills, structured problem solving, relaxation training, breathing retraining, deconditioning, desensitisation, graded exposure, cognitive restructuring
 - Psychodynamic psychotherapy: elucidate mental processes outside the person's conscious awareness so as to alter core conflicts
 - Stop ↓self esteem and manage stigma from having a psychiatric illness
- Secure employment, housing
- Community support: support groups, psych nurse
- On-going review:
 - Plan for follow-up to reassess illness and monitor treatments
 - Identify warning signs for a relapse
 - Plan and prepare for relapses
 - Set and prioritise goals

Genetics and Cancer

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Epidemiology of Genetic Disorders

- 9,000 known genetic diseases
- 5% have genetic diseases before 25
- 60% during lifetime (includes diabetes, heart disease, cancer)

DNA

- There is frequent mutation in rapidly dividing cells: but repair mechanisms ‘mop up’
- If there is a sustained mutation in:
 - Essential gene → lethal
 - Non-coding gene → no effect
 - Non-essential gene → human variability/disease

Chromosome Disorders

- Polyploidy: duplication of whole sets of chromosomes (eg triploidy: n = 69). Non-survivable → fetal wastage
- Anuploidy:
 - One missing or additional chromosome
 - Trisomy 21: 47XY + 21. See Down Syndrome, page 581
 - Trisomy 13: next most common, trisomy
 - Turner’s Syndrome: 45, XO
 - Puffy feet, poor toe nails, redundant skin behind head/neck, kidney and cardiac malformation
 - Later: short, infertile, normal mental ability (unless 2nd X ring chromosome → mental disability)
 - The 10% that survive to term are the good end of the spectrum
 - Differential: Noonan’s Syndrome – similar symptoms but karyotype is normal
 - Klinefelter Syndrome: 47, XXY
 - 1/3 present in childhood with learning difficulty
 - 1/3 present in adolescent: failure of puberty due to no testosterone (ie hypogonadism)
 - 1/3 present in adulthood due to infertility
- Chromosome abnormalities:
 - Deletions, insertions, etc. Will be different in each child → variable presentation. Eg deletion in 5p: Cri du Chat syndrome, cat like cry
 - Fragile X Syndrome: commonest cause of mental disability in males. 1:1,000
- In testing for mosaics, may need to test skin, not blood, as abnormal cells don’t reproduce so well so get weeded out in tissues (eg blood) with high turnover

Patterns of inheritance:

- Autosomal Dominant
 - =Single gene abnormalities expressed in heterozygotes
 - M = F, 50% risk of passing it to kids
 - 1 abnormal gene causes disease
 - Eg Huntington Disease, Marfan Syndrome, Achondroplasia (disturbance of epiphyseal chondroblastic bone formation)
 - But:
 - Variable expression, variable age of onset
 - Non-penetrance happens
 - Gonadal mosaicism (esp if old paternal age) → somatic genes normal, mutation in gonads
- Autosomal Recessive:
 - = Only symptomatic when both alleles at a locus on homologous chromosomes are defective
 - Must have mutations in both genes ⇒ both parent’s carriers
 - Shows up early (no normal genes)
 - Eg cystic fibrosis, phenylketonuria
- X-linked Recessive:
 - Only affects males
 - Impact early (no normal gene)
 - Females are carriers (random X inactivation should mean that 50% of cells are abnormal. But they’re usually in the minority. Still may have some traits)

- Eg haemophilia, Duchenne muscular dystrophy (wasting muscle disease – most dystrophies are X linked)
- X-linked Dominant: eg Fragile X
- Multifactorial:
 - Common diseases
 - Genetic predisposition plus environmental influence
 - Eg Cleft lip/palate
- Others: mitochondrial, tumour predisposition

Non-Mendelian Genetics

Genetic Imprinting

- = Differential expression of genetic material depending on whether it has been inherited from male or female parent
- ⇒ Parent of origin of mutation matters for many genes
- Affected genes are usually highly conserved (ie the same genes appear in mice and humans – conserved through evolution)
- Myotonic dystrophy:
 - Autosomal dominant
 - Progressive weakness from 3rd decade
 - Unstable triplet repeat on 19 (upper limit of normal is 50 repeats)
 - Most unstable when it's from mum (ie parental imprinting)
 - As number of repeats increases goes from normal → premutation carrier → affected
- Fragile X Syndrome:
 - Abnormal if triplet repeat > 200
 - Only expands when passed from mother to son, not to daughter
- Huntington's:
 - Unstable triplet repeat syndrome
 - If father passes it on then greater risk of ↑ number of repeats
 - See Dementia, page 439

Uniparental Disomy (UPD)

- = Presence of a cell line containing 2 chromosomes both inherited from only one parent
- Has been demonstrated in cystic fibrosis, haemophilia (ie got both mutated genes from the one parent)
- Prader-Willi Syndrome:
 - Floppy baby, low birth weight, retarded, ↑↑ appetite → obesity, short stature
 - Caused by deletion on father's Chr 15, or have both normal Chr 15 from mum (ie no 15 from dad)
 - Angelman Syndrome caused by maternal deletion of the same chromosome → low birth weight, unusual cry, stiff legged gait, tremor and seizures

Mitochondrial Disorder

- Mitochondria:
 - Generate ATP for energy using the respiratory chain
 - Contain their own DNA: circular double stranded DNA
 - All come from mother
 - Have higher mutation rate
- Heteroplasmic: up to 200 mitochondria per cell, up to 20 different DNAs per cell
- Usually involves all tissues, very variable expression
- Difficult to test for and hard to treat

Genetic Testing

- Types of test:
 - Screening tests: done on normal population to identify those at risk (not diagnostic)
 - Diagnostic tests to confirm the presence of disease
- Guthrie Card – for screening all neonates:
 - Second test needed in about 1 in 100 babies (usually due to poor sample)

Disease	Treatment	Risk
Biotinidase Deficiency	Take vitamin H (biotin)	1:50,000
Congenital Adrenal Hyperplasia	Steroids	1:20,000
Cystic Fibrosis		1:3,000
Galactosaemia	Diet	1:120,000
Hypothyroidism	Thyroid replacement	1:4,500
Maple Syrup Urine Disease	Diet	1:250,000
Phenylketonuria (PKU)	Diet	1:15,000

- Indications for neonatal genetic testing: Physical, growth or developmental disorders:
 - Still birth
 - Multiple congenital abnormalities
 - Small for age
 - Facial dysmorphia
 - Significant mental retardation
 - Post-natal growth retardation
 - Microcephaly

Other

- Agenesis: complete absence of an organ
- Aplasia: absence of an organ with the persistence of an undeveloped rudiment
- Anencephaly: congenital absence of cranial vault – with cerebral hemispheres completely missing

Genetic Counselling

- Aim: provide information for an individual/couple to make informed choices about their reproductive options, and to assist them in coming to terms with the options they face
- Requires:
 - Diagnostic precision
 - Estimation of risk: either Mendelian or multifactorial (eg cardiac abnormalities, neural tube defects, etc)
 - The likely burden of care for a child with the disorder: variability, life expectancy, quality of life, treatment
 - Alternatives: childless life style, adoption, intrauterine diagnosis, donor sperm, donor ova

Cancer

- See also Childhood Cancer, page 648

Epidemiology

- In NZ:
 - Over 16,000 new cases diagnosed per annum, 7000 deaths
 - Commonest cancers (incidence):
 - Male: prostate, large bowel, lung (incidence ~ mortality)
 - Females: breast, large bowel, melanoma
 - Commonest cause of death:
 - Male: lung, large bowel, prostate
 - Female: breast, lung, large bowel
- Prognosis of cancer is determined by:
 - Tumour related factors: accurate diagnosis, stage, grade, risk factors (eg biochemical markers), cytogenetics
 - Patient related factors: age, sex, co-morbidities

Oncogenesis

- Cancer causing agents:
 - 'Natural' – eg fungus and plant toxins. Eg aflatoxin from fungus contaminating peanuts in Africa → liver cancer
 - Man-made: enormous diversity. Mainly the metabolites/intermediates in the body that are carcinogenic. Very often organ specific. Most precarcinogens detoxified to non-carcinogenic metabolites.

- Cancer = uncontrolled cell proliferation due genetic change
- The more uncontrolled the proliferation, the more mutations – in final stages aneuploidy, translocations, etc will be very common
- Oncogenes: cells related to normal cell proliferation and differentiation. If one allele is mutated then uncontrolled proliferation (\Rightarrow autosomal dominant)
- Tumour suppressor genes: regulatory genes that inhibit cell proliferation. Need to lose both alleles to have an effect (\Rightarrow autosomal recessive)
- Carcinogenesis:
 - Multifactorial – needs multiple DNA mutations
 - P53 Gene:
 - Regulates cell cycle
 - Inactivated in over $\frac{1}{2}$ human tumours
 - Activated by hypoxia, DNA damage, viruses
 - If there is minor cell damage \rightarrow small amount of P53 \rightarrow arrest cell cycle and repair
 - If major damage \rightarrow ↑↑ P53 \rightarrow apoptosis
 - Activated P53 binds to DNA activating other genes
 - Normal P53 can be inactivated by mutating co-factors
 - Philadelphia Chromosome:
 - Arises from balanced translocation t(9, 22)(q34,q11)
 - Brings C-ABL gene beside BCR gene. C-ABL is an oncogene, and is now regulated by BCR \Rightarrow normal regulation has failed
 - Causative in CML, also seen in other tumours. See Chronic Granulocytic Leukaemia, page 298
 - Telomere
 - Non-coding cap to genome
 - During replication, an enzyme binds and prevents replication \Rightarrow telomere shortens with each replication
 - Telomerase can produce telomere – usually only in germ cells. But also active in cancer cells \rightarrow unlimited potential to divide
 - Research aim: find drug to inhibit telomerase \Rightarrow give cancer cells a limited number of divisions
 - Tumour starts with single clone, quickly becomes heterogeneous. Only a few descendants will be able to metastasise
 - Growing tumour needs blood supply – secretes angiogenic factors. Research aim: find ways of inhibiting this process. An advantage would be that this would kill all tumour cells, whereas chemotherapy is selective, leaving resistant cells to grow

Anatomic Pathology and Neoplasia

- Describing a histologic section – always include:
 - Architecture (eg gland formation, infiltration – eg sheet like, cords)
 - Cytologic atypia: hyperchromatic, nuclear pleomorphism, mitotically active
 - Tissue reaction (fibrosis, inflammation, etc)
- Macroscopic signs of invasion:
 - Variegated
 - Poorly circumscribed, not encapsulated, irregular border
 - Crab like
 - Areas of haemorrhage
- Microscopic signs of malignancy:
 - Nuclear pleomorphism
 - Hyperchromatic nuclei
 - Invasion
 - Poorly differentiated (anaplastic)
 - Mitoses
- Tumor prognosis:
 - Stage (how much infiltration, metastasis)
 - Grade (what type, how well differentiated)
 - Resection margin
 - Brisk inflammatory response is good

- Hamartoma = overgrowth of tissue native to that site (NOT clonal proliferation/neoplasm)
- Headings for answering pathology exam essay questions:
 - Incidence
 - Aetiology
 - Pathogenesis
 - Macroscopic description
 - Microscopic description
 - Natural History
 - Outcome
 - Complications
 - Special types

Staging of Cancer

- = Determining the extent of cancer
- Why stage:
 - Affects prognosis
 - Affects treatment
 - Allows comparison of results between centres (eg audit)
- Staging Systems:
 - TNM system:
 - Nomenclature:
 - T: Size and invasion eg 1 = small, 4 = large
 - N: which nodes are involved
 - M: no metastases or metastases present
 - Variations applied to many cancers (eg NSC lung cancer, breast, etc)
 - Guides treatment: eg T1N0M0 → ?wide local excision, T3N1M0 → may start with chemo/RT
 - TNMs are grouped to give stage groups ranging from IA to IV
 - FIGO System: Gynae malignancies, eg cervix:
 - Stage I: confined to cervix
 - Stage II: Not involving the pelvic wall or lower 1/3 of vagina
 - Stage III: extends to pelvic side wall
 - Treatment:
 - I & IIa: surgery or radiotherapy
 - IIb & III: radiotherapy
 - Ann Arbor classification or lymphoma (see Lymphoma, page 305)
 - Dukes Classification for bowel cancer, see Prognosis of Colorectal Cancer, page 174
- How to stage:
 - History: symptoms suggestive of local extension or distant metastases
 - Exam: nodal involvement, metastatic involvement (bone tenderness, hepatomegaly)
 - Bloods: FBC (blood loss, marrow involvement), LFT, ALP and albumin (liver involvement), tumour markers
 - Imaging:
 - CXR, mammography
 - CT Scanning – to determine primary disease, nodal involvement
 - MRI: especially CNS and spinal chord tumours
 - Nuclear medicine: bone scan
 - US: good for differentiating cystic from solid, especially in the abdomen
 - Contrast studies (barium swallow, enema): largely surpassed by endoscopy
 - Special investigations:
 - Bone marrow: lymphomas, small cell lung
 - FNA: either US or CT guided
 - Laparoscopy: node sampling
 - Endoscopy
 - Surgery: role in staging tumours largely overtaken
- Tumour markers:
 - Generally only reliable for monitoring treatment in cancer demonstrated to produce a tumour marker. Generally poor for screening

- β HCG: germ cell tumours. Used for diagnosis and monitoring treatment
- AFP: produced during liver regeneration: hepatocellular cancer, testicular embryonic cancers, yolk sac tumours
- CEA: produced by epithelial elements (colon, ovary, pancreas). Usually in advanced disease so no use for screening. Also in gastritis and UC
- CA125: ovarian cancer (good response marker). Also in endometriosis, hepatitis
- PSA: levels correlate well with disease extent. $> 10 \Rightarrow 80\%$ chance of cancer

Cancer Treatment

- Treatment objectives:
 - Cure
 - Prolong life expectancy
 - Relieve symptoms
- Treatment modalities:
 - Chemotherapy
 - Radiotherapy
 - Symptomatic/Supportive
- For Treatment of:
 - Colorectal cancer, Treatment of Colorectal Cancer, page 173
 - Breast cancer, see Treatment of Breast Cancer, page 381

Radiotherapy

- Superficial X-ray: for skin cancers
- Cobalt: no longer used in the west. Max 1.2 MV
- Linear accelerators:
 - 6 MV to 18 MV
 - Skin sparing
 - Produces electrons and photons. Biological effect of photons is to create free radicals
 - Does lots of damage to the cell – but only damage which affects reproductive integrity is DNA damage
 - Most DNA damage is repaired within 6 – 8 hours, but if lots of damage then non-repair
 - More damage is done to cells in G2 (ie in mitosis) as DNA is super coiled
- Effective use requires:
 - Good planning: how to maximise dose to the lesion while minimising dose to unaffected tissue
 - Immobilising the patient
- Use of multiple fractions (ie lots of small doses) spares normal tissue as this has time to repair, but tumour tissue doesn't repair so well
- Uses:
 - Aim is curative in head and neck, skin, cervix
 - Anal (with chemo), rectal (with surgery)
 - Adjunct in lung, stomach cancer
- Toxicity:
 - Acute: builds up during treatment and settles within ~ 6 weeks
 - Affects rapidly dividing cells and secretory function
 - Skin: erythema, desquamation
 - Mouth: mucositis and dryness
 - Gut: diarrhoea, colic, ileus
 - Bladder: cystitis
 - Marrow (only if widespread dosing): leukopaenia, thrombocytopenia
 - Late: Months to years
 - Due to healing with fibrosis or ↑aging of tissues
 - Affects slowly or non-dividing cells and causes permanent damage
 - Skin: Telangiectasis, fibrosis
 - Mouth: Dryness (\downarrow parotid function), caries, osteoradionecrosis
 - Gut: stricture, fistula
 - Bladder: contracture, haematuria
 - Nerves: myelitis, necrosis, neuropathy

Chemotherapy

- Systemic treatment with single or multiple agents
- Damages DNA/RNA protein synthesis → cell death/apoptosis. Not tumour specific
- Predictable side effect depending on the schedule. Side effect management has improved greatly
- Can be oral, sc, im, iv, continuous iv
- Adjuvant Treatment = after local therapy has removed cancer but where there is a statistical chance of relapse (eg due to micro metastases)
- Uses:
 - Can be curative in: lymphoma (esp Hodgkin's), leukaemia (including ALL), sarcomas of childhood, Germ cell tumours (Testicular teratoma, Seminoma), etc
 - Adjuvant in breast, large bowel and ovarian cancer
 - Prolongation of life: Ovarian, lung (small cell lung cancer is sensitive to chemotherapy), bowel, breast
 - Relief of symptoms: shortness of breath, pain/discomfort, local disease
 - Not in melanoma, renal cell carcinoma
- Side effects:
 - General:
 - Feeling terrible till 2 – 3 days later
 - Nausea: 5HT3 antagonists to help
 - Lethargy, anorexia
 - Affect on fast growing tissues:
 - Mucous membranes: mouth ulcers, diarrhoea
 - Hair loss: not inevitable (depends on regime) but always temporary
 - Bone marrow: myelosuppression, anaemia, neutropenia, thrombocytopenia
 - Irritant effects: haematuria, sore eyes
 - Neutropenia: typically 1 – 3 weeks following. See Fever in a Neutropenic Patient, page 301
 - ↓Fertility (especially in men) but no risk of future fetal abnormality (unless pregnant at the time). NOT a reliable contraceptive

Other treatment options

- Hormones
- Immunotherapy

Symptom Management in Cancer

- See also Constipation, page 177

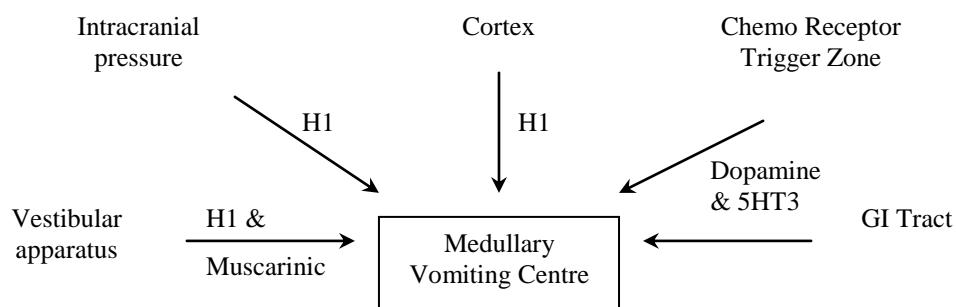
Pain Management in Cancer

- See also Pain Management, page 543
- Principles of symptom control:
 - Evaluation: identify each problem/pain and make sure it's managed
 - Explanation
 - Individualised treatment
 - Monitoring progress
 - Attention to detail
 - Anticipate problems
- Common problems:
 - Physical symptoms: pain, anorexia, nausea, insomnia etc
 - Compounded by anger, losses, fear, financial insecurity, anxiety, isolation, bewildered by treatment. Always consider emotional, intellectual and spiritual components
- Causes of pain:
 - Destructive/obstructive effects of the cancer
 - Debility: pressure sores, constipation
 - Due to treatment
- WHO analgesic ladder:
 - Step 1: mild pain. Paracetamol, aspirin, NSAIDs
 - Step 2: moderate pain. Codeine, Tramadol (not subsidised, plus combination drugs:
 - Paradex (Digesic): dextropropoxyphene plus paracetamol
 - Panadine: codeine plus paracetamol

- Step 3: severe pain:
 - Morphine:
 - Actions: analgesia, respiratory depression, drowsiness, vomiting, miosis, convulsions, euphoria or Dysphoria, smooth muscle stimulation (\rightarrow GI muscle spasm, biliary and renal tract spasm)
 - Rapid acting oral: morphine elixir (10 mg 4 hourly) or Sevredol tablet (10 or 20 mg): maximum effect after 2 hours
 - Longer acting: MST (duration 8 – 12 hours) or Kapanol (24 hour slow release)
 - PR: rapid acting suppositories or MST
 - Parenterally: IM (onset in 10 – 15 minutes, lasts 4 hours), SC, IV
 - Bioavailability: half parenteral dose over oral
 - Anticipate constipation
 - Signs of morphine overdose: RR < 12, if RR < 8 then Naloxone
 - Methadone (difficult titrating the dose)
 - Fentanyl: less constipation than morphine, but not subsidised, transdermal fentanyl patches lasting 72 hours are well suited to patients with stable pain and low to medium opioid requirements
- Adjuvants at any stage: TCAs, anticonvulsants, steroids, muscle relaxants, antiarrhythmics
- Anticipate pain and give regular analgesia, plus PRN medication for acute-on-chronic pain ('breakthrough' pain)
- Enhance coping skills:
 - Listen and acknowledge the symptoms
 - Explanation, information
 - Shared decision making
 - Calm supportive environment
 - Complementary therapies: relaxation, art therapy, music, OT diversional therapy
 - Spiritual support, counselling
 - Treat anxiety, depression
 - Support the family

Management of Nausea

- Identify the right pathway and treat it specifically:



- “Drugs of choice”:
 - H1 antagonist: cyclizine
 - D2 antagonist: Haloperidol
 - Prokinetic: Oral domperidone, iv metoclopramide (also has anti-D2 effect)
- Chemical cause (stimulation of chemoreceptor trigger zone by uraemia, opioid induced, hypercalcaemia, toxins): stimulates dopamine receptors. Haloperidol is a dopamine antagonist, as is chlorpromazine, metoclopramide and cisapride
- Mechanical cause (squashed stomach, delayed emptying, regurgitation): Metoclopramide and domperidone \rightarrow prokinetic action
- Emetogenic chemotherapy: stimulates release of serotonin in the gut: 5HT3 antagonists are used (ondansetron, granisetron, tropisetron)
- Vestibular and \uparrow ICP: use antihistamines eg cyclizine
- Non-drug therapy: prophylactic treatment of constipation, keep away from sight or smell of food; small, frequent, attractive meals, relaxation therapy, acupressure

Management of Breathlessness

- Due to effusion, anaemia, mass or irritant effect, anxiety, fatigue. Compounded by fear of fighting to breath. Can also be PE (but don't anticoagulate them – it's better to die from a clot than a bleed)
- Low dose morphine → ↓irritant respiratory reflexes
- Anxiolytics for panic (eg lorazepam for intermittent breathlessness, diazepam for chronic)
- Steroids for anti-inflammatory effect
- Nebulised saline: shift sticky secretions, humidify dry airways
- Oxygen if symptomatic hypoxia – but commits the patient to the equipment
- Advice from physio, especially re controlling expiration
- Fan on face, open window

Management of Cachexia

- = Marked weight loss and muscle wasting, especially in advanced GI and lung cancers
- Due to ↑metabolic rate and ↓food intake, plus abnormal metabolism and cytokine production
- May also see altered taste sensation, loose dentures causing difficulty eating, oedema due to hypo-albuminaemia, pressure sores over bony prominences, etc
- Body changes may generate feelings of fear, isolation or difficulty with relationships
- Management:
 - Dietary supplements and NG feeding are unlikely to achieve anything. Patients should eat and drink as they wish
 - Corticosteroids in a reducing protocol may help (as well as reducing tumour oedema)
 - Relining dentures
 - General support: education, new clothes, aides to maintain independence

Cancer Emergencies

- See also Fever in a Neutropenic Patient, page 301
- Spinal Cord Compression:
 - Irreversible damage occurs quickly. Even if poor prognosis from cancer mobility makes a key difference to quality of life and to ease of nursing at home, etc
 - Symptoms: pain (often dermatomal at the level of the lesion), weakness, autonomic dysfunction, sensory loss
 - 95% is extramedullary compression. Thoracic > lumbosacral > cervical
 - Primary tumours: lung, breast, prostate, lymphoma (very radiation sensitive), myeloma, kidney
 - Differential: infective or mechanical
 - Contraindications to Radiotherapy: previous RT (already irradiated to spinal tolerance), radio-resistant tumour (eg myeloma), no tissue diagnosis (ie don't know what you're treating)
 - Contraindications to surgery: widespread systemic disease, multiple levels, vertebral body collapse, known radio-sensitive tumour
 - CXR usually done but MRI is investigation of choice
- Cauda Equina syndrome
- Superior Vena Cava Syndrome:
 - Compression causing thoracic and neck vein distension, facial and arm (maybe unilateral) oedema
 - Causes: CNS symptoms (Headache, visual disturbance, dizziness, blackout, altered conscious state), venous thrombosis
 - Usually due to lung cancer, also lymphoma and metastases. Benign causes include goitre, fibrosis, sarcoidosis, syphilis, etc
 - Investigations: examination, CXR, CT (rather than MRI), biopsy (maybe US guided)
 - Treatment:
 - Anticoagulant + thrombolysis if established clot (eg neck veins not compressible)
 - Endovascular stent if recurrent
 - Chemotherapy: small cell lung cancer (80% response), Hodgkin's Lymphoma or Non-Hodgkin's lymphoma
 - Radiotherapy: any other malignant cause (80% response)
- Hypercalcaemia: stones, groans and moans, also thirst. Tx: Rehydrate + Bisphosphonates
- Pathological fracture: orthopaedic referral to stabilise
- Haemorrhage: tumours bleed easily, erosion into an artery
- Obstruction:
 - Trachea → stridor. Mainly extrinsic compression. Options: RT, steroids (↓oedema), tracheostomy

- Bronchus: dyspnoea
- Oesophagus: Dysphagia. Usually progressive not an emergency. Lodged bolus can present acutely
- Bowel
- Ureter

Palliative Care

- See also Grief and Bereavement, page 458
- Palliative Care: care of patients with active, progressive, far advanced disease and a limited prognosis and for whom the focus of care is the quality of life
- Regards death as a normal process
- Integrates physical, emotional, social, cultural and spiritual aspects of care
- Offers support to help families and care givers
- Provide relief from pain and other distressing symptoms
- Neither hastens nor postpones death

Emergency Management

-
- References: A New Zealand Guide to Resuscitation Practice, Wellington School of Medicine, New Zealand Resuscitation Council.

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Resuscitation

- Objective: keep oxygenated blood flowing to the brain – otherwise cell death in 2 – 4 minutes
- Basic life support = no special equipment
- Advanced life support = basic support + equipment + drugs
- Early defibrillation is vital: increasingly non-doctors are being trained to use it outside hospital setting

Cardiopulmonary Resuscitation (CPR)

Summary

- Ensure safety
- Check responsiveness
- Send for help
- Open Airway
- Check breathing/circulation: no longer than 20 seconds
- Precordial thump (if arrest within last 90 secs)
- Go for help
- 2 Effective Breaths – up to 5 attempts
- Chest compression/ventilation: adult 2 breaths per 15 compressions at 100 bpm, neonates 1 breath per 5 compressions 100 bpm
- ASAP: attach monitor Defibrillator and assess rhythm
- VF or VT or AED ‘shock advised’:
 - Defibrillate: 200, 200, 360J (3 * 360J thereafter)
 - Adrenaline every 3 minutes
 - 1 minute CPR
- Not VF or VT or No Shock Advised
 - Adrenaline
 - 3 minutes CPR
- Reassess rhythm or circulation

Adjunct Priorities:	Advanced Adjuncts:	Check:	Consider and Correct:
<ul style="list-style-type: none">• Defibrillation• Advanced airway/ ventilation adjuncts• Oxygen• IV access	<ul style="list-style-type: none">• Endotracheal Intubation• Laryngeal Mask airway• Adrenaline: 1mg/3 minutes• VF/VT: Defibrillation, Lignocaine 1mg/kg after 3 loops• Asystole: atropine 3 mg• Consider: pacemaker, buffers	<ul style="list-style-type: none">• Defibrillator/ECG: source, settings and electrodes• Endotracheal/IV placement	<ul style="list-style-type: none">• Hypoxia (give O₂)• Hypovolaemia (give colloids, saline)• Hyper/hypokalaemia (give Ca/K)• Hyper/hypoglycaemia (give insulin & K/glucose)• Hyper/hypothermia (cool/warm)• Tension Pneumothorax (chest drain)• Tamponade (pericardiocentesis)• Toxicity• Thromboembolus

A – Approach, Assess, Airway

- Ensure own safety, summon help
- Assess for responsiveness (gently shake, shout, be careful of other injuries). An arrest may present as a short grand mal seizure
- Cervical spine injury should be suspected, and assumed in unconscious patient esp. trauma. However, airway management takes precedence
- Urgent airway support may be indicated by: respiratory distress, hypoventilation, absent response to pain or stimuli, major skull, face or neck trauma, chest injuries, high spinal cord injury
- Open airway: CNS depression will diminish muscle tone in upper airway → tongue and epiglottis will obstruct airway → further hypoxia (faster in kids due to higher metabolic rate)
- Tilt head back, chin lift, jaw thrust

Airway Management Techniques

- Oropharyngeal airway insertion:
 - To maintain airway or prevent biting
 - Use Geudal airway. Male size 4, female size 3

- If they tolerate oropharyngeal airway without gagging or coughing \Rightarrow no protective reflexes and need to be endotracheally intubated as soon as practical to protect from aspiration
- Laryngeal mask insertion:
 - For failed endotracheal intubation where Positive Pressure Ventilation indicated
 - Doesn't protect from aspiration
 - Male size 4, female size 3
- Endotracheal intubation:
 - For control of airway, ventilation, protection from aspiration and prevention of gastric distension (e.g. in bag mask ventilation)
 - Sizes: Adult male size 9, female size 8, child (age in years)/4 + 4
 - If conscious and struggling may require sedative (e.g. thiopentone) and relaxant (suxamethonium)
 - Always check chest movements and CO₂ return to check you haven't got it in the oesophagus
 - Watch for pressure necrosis of tracheal mucosa from too large a tube or \uparrow inflation
 - Never attach O₂ directly to tube (\rightarrow over inflation) – always via a ventilation/bag mask system
- Bag mask ventilation (AMBU Bag)
 - Always check chest rising: watch for leaks around mask, check patent airway
 - Too much pressure \rightarrow gastric distension and aspiration into unprotected trachea
- Cricothyrotomy:
 - Use to gain access to airway where other methods have failed
 - Clean skin with antiseptic solution
 - Find cricothyroid membrane, between thyroid cartilage and cricoid ring immediately below it
 - Make horizontal incision through membrane. Insert handle of scalpel into incision and rotate 90 degrees
 - Insert largest possible endotracheal tube and attach to ambu bag. Ventilate with O₂
 - Alternatively, use size 14 cannula, at angle of 45 degrees pointing down towards lungs. Attach cannula to syringe and syringe to ambu-bag

B – Breathing

- Ear over mouth and nose and look for chest to rise and fall. Slow gasping respirations may persist after arrest but these are ineffectual
- Assess whether trachea central, breath sounds bilateral, and check for crepitus (\rightarrow ?pneumothorax)
- Exclude life threatening chest injuries: tension or open pneumothorax, flail segment

C – Circulation

- Check carotid pulse.
- Look for signs of circulation: movement, colour, etc

Action Plan

- If breathing and circulation but unconscious \rightarrow recovery position, and maintain airway
- If not breathing but there is circulation \rightarrow ventilate with 10 expired air ventilations over a minute and reassess
- If chest moving but there is no flow of air then obstruction \rightarrow head tilt, chin lift, jaw thrust forward
- If breathing absent or deteriorating and no or unsure of circulation then presume arrest
- Commence CPR/defibrillation, but consider (if you can):
 - Use O₂ if at all possible – they will be hypoxic. Cylinders are black with white shoulder. Connect to ventilation bag at 4 atm. or to mask if breathing spontaneously (minimum 4 – 5 L per minute). NEVER connect directly to endotracheal tube (would \rightarrow barotrauma)
 - Gaining iv access e.g. antecubital vein. Give saline flush after each access and hold limb up (circulation will be sluggish). Nothing more distal on arm, and don't use femoral (unless needed for fluid replacement in trauma). If can't get access, use carotid (subclavian interferes with CPR), or down endotracheal tube (2 to 2.5 times iv dose) with 10 ml saline

Adult CPR

- If defibrillator available, consider immediate use
- If no defibrillator and arrest has occurred within 90 – 120 seconds then single precordial thump – may convert ventricular arrhythmias in small number of cases, should never break bones, never in presence of palpable pulse (as may cause VF if delivered on T wave – commotio cordis)
- Get help: it is most likely a VF (and other things have a poor prognosis) and you need to defibrillate
- Continue with cycles of:

- 2 expired air ventilations (mouth to mouth or nose, normal not big breath otherwise inflate stomach → gastric reflux, allow time for expiration). Theoretical risk of infection → take precautions
- 15 chest compressions:
 - Raise legs → ↑venous return
 - Press over junction of middle and lower thirds of sternum
 - Use only heel of hand with thumb side lower
 - Lock elbows, push straight down, move from hips not shoulders. Get on bed if you're too low
 - Consider putting board under patient or place on floor – soft mattress will impair compression
 - Depress 4-5cm or one third of chest thickness: it is depth not force that is important, equal compression and relaxation times, not too jerky. Start gentle to determine correct pressure. Rib fractures impede filling, cause pneumothorax, lacerations of liver and spleen, and fat emboli
 - Rate of 100 per minute for adults and children.
 - Can achieve systolic pressure of 60 – 80 mmHg, but low diastolic pressure so brain perfusion maintained but heart perfusion poor. Adrenaline improves diastolic pressure
- If two operator, still use 2:15 breaths per compressions. If patient not intubated pause 1 sec for ventilation. No pause necessary if intubated
- After 3 minutes, stop for 10 secs to assess circulation. Continue with assessments every 3 minutes until defibrillator arrives
- Administer adrenaline 1 mg iv with every 3 minute loop

Paediatric CPR

- Respiratory distress/failure much more common cause of cardiac arrest than cardiac problems. Hypoxia and global ischaemia therefore often precede arrest (in adults it follows arrest), which results in asystole – not VF. Also caused by hypovolaemia, poisoning, drowning, etc
- Ventilation therefore more important than defibrillation. Kids have a higher metabolic rate and O₂ reserves consumed quicker
- Survival associated with duration of arrest (after 5 minutes it plummets), not more than one dose of adrenaline, and presence of VF
- Procedure:
 - Ensure your and patient's safety
 - Assess responsiveness. Don't shake a baby. If unresponsive, shout for help
 - Open airway: head tilt (not too much extension) and chin lift. Jaw thrust instead if cervical trauma. Check for obstruction
 - Assess breathing. If chest moves but no breath, recheck airway
 - Ventilate: 5 attempted breaths 1 – 1.5 seconds. In babies and infants, give through nose or nose and mouth. Slow breaths at low pressure better than fast/high pressure (↓gastric distension). Ventilate just sufficiently to make chest rise and fall
 - For no more than 10 secs, check circulation. Infants: brachial, femoral, axillary arteries or apex beat. If over 8, carotid best
 - If no circulation or less than 60 bpm, external chest compression. Over junction of middle and lower 3rd of sternum.
 - In neonates, use two fingers to depth of 1 – 1.5 cm. Rate of 100 bpm, ratio of compressions to ventilations is 5:1
 - Kids over 5, heel of one hand, depth approx. 2 – 3 cm
 - Larger kids, two handed compression, depth of 3 – 4 cm, rate of 80 – 100 bpm, and ratio of 15: 2
 - After one minute alert emergency services
 - Resume CPR: reassess circulation after 3 minutes. Give adrenaline. If iv access time consuming, then 18 gauge perpendicular into anterior surface of tibia, 1 – 3 cm below tibial tuberosity. Failing this, give 10 times iv dose down endotracheal tube. Repeat cycle and adrenaline
 - When defibrillator arrives, assess rhythm. Use paediatric paddles if < 10 kg. ONLY if rhythm is VF or VT deliver 3 shocks at 2, 2, then 4 joules per Kg. Perform CPR for one minute, reassess rhythm. Every 2nd loop give adrenaline
- Ventilation: Harder in kids – use two people to do bag-mask. Beware of barotrauma
- If hypovolaemia → 20 ml/kg saline or Ringers

Defibrillation

- Produces a simultaneous depolarisation of myocardial fibres → allows coherent rhythm

- Ideally within 90 seconds, preferably within 8 minutes. DON'T delay defibrillation to allow period of CPR
- Apply ECG monitor
- Switch on defibrillator (do this in transit)
- Check its NOT in synchronised (cardioversion) mode
- One paddle (doesn't matter which) to right of upper sternum below the clavicle
- Other paddle just to the left of the normal apex beat
- Use a conducting aid (either electrode gel or pads), wipe up any gel that may short circuit between the pads
- First, use paddles to assess rhythm (check settings on defibrillator). Classify as:
- Ventricular fibrillation or ventricular tachycardia (wide QRS complex):
 - Charge defibrillator to 200J (for kids 2J/kg). This is low, but will charge quicker and do less damage to myocardium
 - 'Stand clear': make sure you're not touching patient or bed
 - Recharge defibrillator
 - Observe ECG
 - If VT or VF persists, deliver a second 200J shock, then 360J
 - If VT/VF persists, 1 minute of CPR (attach ECG leads during this, insert artificial airway, iv access etc)
 - Repeat sequence, but with 360, 360, 360 then 1 minute CPR
 - Adrenaline, 1 mg, with every 2nd loop (i.e. every 3 minutes)
 - If following a shock an organised rhythm appears which could be associated with cardiac output, check circulation. If absent then 3 minutes of CPR
 - If following a shock, the rhythm changes from VF/VT to asystole, perform 1 minute CPR and assess with NO adrenaline. 'Stunned myocardium' may take 20 – 30 secs to start again
- Another rhythm. If asystole or electromechanical dissociation (if normal complex) then continue CPR in 3 minute loops, 1mg adrenaline per loop. Prognosis poor but consider:
 - If asystole, is there an electrical fault, low gain on ECG. If in doubt deliver 3 defibrillating shocks
 - If asystole with P waves (ventricular standstill) consider emergency transcutaneous electrical pacing
 - Atropine, 3 mg iv, provides complete vagal blockade, as profound bradycardia may result from intense vagal over activity
 - Treatment of precipitating condition

Cardioversion

- Is timed via ECG to occur on the R wave – must avoid the T wave (otherwise can → VF)
- Is used for:
 - Ventricular tachycardia where pulse is present,
 - Supraventricular dysrhythmias (SVT, atrial fibrillation, atrial flutter)
- Won't fire unless it can detect the QRS. So if trying to defibrillate and it's not working – check defibrillator is not set to cardioversion

Cardiac Arrest Rhythms

- See also Arrhythmias, page 40
- Due either to:
 - Disordered electrical activity (arrhythmia) such as following an MI, or
 - Impaired mechanical performance: Pulseless Electrical Activity (PEA) or Electro-Mechanical Dissociation (EMD) – primary (damaged myocardium, e.g. ischaemia) or secondary (e.g. hypovolaemia, pneumothorax, anaphylaxis → ↓afterload, pulmonary embolus). EMD has worst prognosis. ECG may be normal but patient is still arresting

Ventricular Fibrillation (VF)

- Most non-traumatic arrests are ventricular fibrillation. Only effective treatment is defibrillation
- No organised depolarisation → doesn't contract as a unit. But still contracting ⇒ still using O₂
- Coarse VF: irregular, large amplitude ECG waves → onset recent. Responds well to defibrillation (if given within 5 – 8 minutes). CPR not sufficient to maintain the coronary artery perfusion necessary to offset O₂ consumption → rapid ischaemia. Precordial thump MAY revert VF
- Fine VF: progressively lower amplitude VF until indistinguishable from asystole. 5-10% decrease in likelihood of successful defibrillation per minute

- Treatment:
 - Defibrillation
 - CPR and adrenaline help maintain diastolic BP and thus ↑ cardiac perfusion
 - If failing, consider sodium bicarbonate and lignocaine (antiarrhythmic)
 - Discontinue after 30 minutes

Ventricular Tachycardia

- Fast (100 – 220/minute) and wide QRS complexes (> 0.12 sec)
- Causes: ischaemia, K or Mg disturbances, PE, etc
- Can be confused with supraventricular tachycardia with bundle branch block
- Dangerous precursor of VF
- Treatment:
 - If stable (i.e. still sufficient cardiac output → pulse):
 - Oxygen
 - Lignocaine (1 mg/kg) stat plus 0.5 mg/kg every 8 minutes up to 3 mg/kg
 - If this fails then cardioversion
 - If little cardiac output/no pulse: same as for VF
 - If pulse but unstable:
 - Sedation
 - Cardioversion: starting at 50J, then 100 then 200 then 300. If recognisable regular rhythm then synchronised
 - If recurrent, give lignocaine, then procainamide 20 mg/min up to 1000 mg then bretyllium 5 – 10 mg/kg and magnesium

Torsade de Pointes

- ECG like VT – but QRS amplitude changes due to rotating electrical axis
- May be self-limiting for periods of 5 – 10 secs
- May be due to anti-arrhythmics prolonging the QT interval (if so, stop them)
- Treat by correcting electrolyte abnormalities and by increasing basic heart rate (i.e. over-pacing)
- Magnesium sulphate 1-2gms given over 1 – 2 minutes may reverse drug induced torsade
- Defibrillate for sustained episodes or use over-drive pacing

Asystole

- Complete absence of ventricular electrical activity
- Usually end result of major disturbance/myocardial damage
- Usually a wandering straight line (if completely flat check ECG)
- Invariably fatal after 15 minutes
- Atropine + CPR may bring back rhythm

Drugs in Cardiac Arrest

- No drug has been shown to consistently improve patient survival after cardiac arrest. CPR, defibrillation and airway control are therefore most important
- Adrenaline: peripheral vasoconstriction raises afterload, aids cardiac perfusion in diastole during CPR. Short duration of action → give 1 mg every 3 minutes. For kids, 10 µg/kg, subsequent doses 100 µg/kg. Effect wears off as local mediator dilator effects predominate in distal arteries
- Sodium bicarbonate: but major acidosis is usually respiratory, in which case bicarbonate → ↑CO₂ so will make this worse. Consider after prolonged hypoxia. Also in severe ketoacidosis. Don't give via endotracheal tube
- Lignocaine, 1 mg/kg: for ventricular ectopy and stable ventricular tachycardia. No clear evidence of value in VF. ↑Shock energy required for successful defibrillation. Makes VF less likely – but harder to get out of
- Calcium: if massive blood transfusion will be calcium depleted

Care Following Arrest

- Transfer to ICU or CCU
- May need short period of elective ventilation
- Monitor cardiac rhythms, urine output, cerebral oedema, acid-base balance
- Prognosis of neurological function often clear from 24 hours after arrest

Secondary survey

- Check BP, respiratory rate, temperature
- Check for palpable pulse, capillary return to compressed fingernail bed, and neck veins
- Work systematically from head, to chest, abdomen, pelvis.
- Check limbs and vertebrae for fractures
- External haemorrhage: pressure bandages, splints for fractures, if Military Anti-Shock Trousers (MAST) used for pelvic/femoral fracture, should only be very temporary and let down slowly (to avoid hypotension)
- Non-obvious injuries to exclude (as they may be life threatening): aortic dissection, pulmonary contusion, spinal injury, penetrating wounds (esp to back), and intra-abdominal bleeding (e.g. if persisting shock)
- Complications can occur insidiously: hypothermia, acidosis, sepsis, coagulopathies, shock
- Need 2 iv access sites with 14 gauge: arms, femoral, jugular, saphenous, subclavian vein, or cutdown to medial basilic or long saphenous vein (1 cm anterior to medial malleolus). Intraosseous in infants
- Fluid replacement: warmed crystalloid (watch for cerebral oedema) or colloid, blood where indicated.
- Monitor pulse, BP, skin colour, capillary refill and urine output
- Check for neurological disability
 - Very common, esp in road trauma
 - Check: Alert, responding to vocal stimuli, pain, or unresponsive
 - Moving limbs doesn't exclude spinal injury
 - Check pupils

Glasgow Coma Scale (GCS)

- Eye opening: E4 spontaneous, E3 to speech, E2 to pain, E1 nil
- Verbal response: V5 orientated, V4 confused conversation, V3 inappropriate words, V2 incomprehensible sounds, V1 nil
- Best motor response: Obeys M6, localises M5, Withdraws M4, Abnormal flexion M3, Extension M2, M1 Nil
- 8 or less = severe head injury
- There is also a trauma score, includes GCS, respiratory rate, respiratory expansion, systolic BP and capillary refill

Diagnosis of Death

- Must be made by a doctor
- Must have all of: no respiration, no BP, no HR, no pupillary reflex, no response to pain

Resuscitation Ethics

CPR Efficacy

- Wide variation in outcome depending on clinical circumstances. Discharge rate is 15%. Biased by large number of 'futile' resuscitations.

	Outcome	Comment
Elective cardiac surgery	100%	Heart deliberately stopped
Out of hospital arrest, immediate CPR, ambulance < 2 min	80%	Early defibrillation key predictor of survival. Survival ↓ by 10% per minute.
Arrest under anaesthesia	20%	Would already have had severe physiological assault prior to arrest
Out of hospital arrest, no CPR, ambulance > 6 min	< 6%	
Malignancy, severe chronic disease, chronic renal failure, pneumonia, trauma	< 5%	

- Poor outcomes (e.g. brain damage, organ failure) are inversely correlated with chances of survival.
- Age per se is not an independent predictor of survival after CPR – but is correlated with illness

CPR and Consent

- Family members are not able to give consent (either for treatment or withdrawal treatment) under common law in NZ, although H&DC Code has provision for taking into account "the views of other suitable persons who are interested in the welfare of the consumer..."

- Doctor must make a ‘substituted professional judgement’: immediate decision on available information (usually not much) of what is in the patient’s best interests
- Ethically wrong to undertake resuscitation in patients in whom it is possible to predict a very low rate of intact survival
- Futile treatment diverts resources from other people. It is the principle of justice not the principle of autonomy that creates a right to treatment
- Doctor’s should not make decisions based on their assessment of the patient’s quality of life. Only the patient can make this assessment. However, this information is not usually available in acute setting. Revise further resuscitation/treatment decisions when this becomes available (i.e. the decision to resuscitate or not is not static)
- There is no ethical difference (may be other differences) between withholding and withdrawing treatment. Can revise decision to resuscitate as the probability of poor outcome grows or other information (e.g. patient’s wishes) comes to light

DNR Orders

- = Do not resuscitate, DNAR = Do not attempt resuscitation
- Reasons for DNR orders:
 - Refusal by a competent and informed patient
 - Poor quality of life after CPR (patient’s, not doctor’s view)
 - Futility: a clinical decision – so should the patient be involved or not?
- DNR orders should be discussed where:
 - Requested by a competent patient
 - Considered on grounds of poor quality of life
- Circumstances where it is not necessary to discuss DNR orders:
 - Patient is incompetent
 - Competent patient but grounds of quantitative futility
 - Where discussion of CPR would be detrimental to patient’s well being
 - Where patient indicates they do not wish to discuss CPR
- Role of family/friends: get their input, but doctor makes the decision regarding CPR unless the patient has a welfare guardian or has an advance directive
- Other points:
 - A DNR doesn’t mean other treatment is withdrawn
 - DNRs must be clearly documented in notes, including discussion of decision making process
 - DNRs should be reviewed regularly and may be withdrawn if warranted by change in clinical circumstances

Shock

Clinical Signs

- CNS: agitation, anxiety, confusion, changed consciousness, convulsions, focal signs, pupillary dilatation
- Respiratory - ↑RR, ↑respiration effort, ↑cyanosis, SOB, cough
- CVS - ↑HR, ↓BP, ↓pulse pressure, ↓capillary return, pallor, sweaty, cool extremities, arrhythmias. Systolic BP < 90 and HR > 100. Treatment should aim to keep BP above 80 mm Hg
- Renal - ↓urine output (< 30 ml/hour or < 0.5 ml/kg/hr)
- Cutaneous: flush, angioedema (swelling of face/mouth)
- GI: abdominal cramps, diarrhoea, vomiting, urinary/faecal incontinence
- See Adult Respiratory Distress Syndrome (ARDS), page 83

Septic Shock

- Systemic Inflammatory Response Syndrome (SIRS) is the presence of 2 or more of:
 - Temp $\geq 38^{\circ}\text{C}$ or $< 35^{\circ}\text{C}$
 - HR $+ 90 \text{ bpm}$
 - RR $\geq 20/\text{min}$ or $\text{PaCO}_2 \leq 32 \text{ mmHg}$
 - WBC $> 12,000 \text{ cells/ml}$
- Septic shock evolves from SIRS when BP $\leq 90 \text{ mmHg}$ despite adequate fluid but need e.g. an inotrope to raise BP
- Hyperdynamic circulation: may present early on with warm peripheries because of mediator-induced vasodilation – confusing as they’re not cold and clammy

- Infection: 70% due to G -ive: endotoxin release → inflammatory mediators → SIRS → changed haemodynamics
- Management:
 - O₂ + ventilation
 - Circulatory support
 - Nutrition
 - Treat infection
- Mortality = 30 – 40 %

Cardiogenic Shock

- Causes
 - MI or ischaemia: need to lose 40 – 50% of functional ventricular mass
 - Trauma
 - Cardiomyopathy/myocarditis
 - Dysrhythmia
 - Valvular/septal defects
 - Post cardiac surgery: stunned myocardium
 - Drugs
- ↓Contractile mass → ↓CO → shut down → hypoxia, ↓LVEDP → pulmonary oedema (more acute than heart failure)
- Management
 - Maximising coronary perfusion: ↓ afterload, maintain CO (inotropes), vessel patency (drugs, stents, etc), intra-aortic balloon pump
 - Treat other factors: dysrhythmias, hypertension
 - Support organ failure

Hypovolaemic shock

- Causes:
 - Blood loss (usually trauma)
 - GI (vomiting, diarrhoea)
 - Renal (diuretics)
 - Surface (burns)
 - Maldistribution (e.g. sepsis, anaphylaxis)
- Estimated losses from fractures:
 - Femur: 1000 – 1500 mls
 - Pelvis: 1500 – 2500 mls (usually venous)
 - Tibia and fibula: 750 – 1200 mls
 - Humerus: 500 – 750 mls
 - Also chest, abdomen, retroperitoneum, scalp
- Management: ABC, O₂, iv fluids, minimise losses
- Initial bolus for paediatric shock is 20 ml/kg

Severe Anaphylaxis

- = Severe allergic reaction
- See also Allergy and Hypersensitivity Disorders, page 309
- Problems:
 - Acute CV collapse: hypotension, myocardial ischaemia, arrhythmias
 - Lower airway: Bronchospasm → respiratory difficulty. Respiratory problems account for 70% of fatalities. Asthmatics at higher risk.
 - Upper airway: Laryngeal oedema (ie angioedema)
 - Also skin problems (urticaria, erythema, itch), nausea, vomiting, diarrhoea, anxiety, etc
- Pathogenesis:
 - Type 1 allergic reactions mediated by IgE antibodies
 - Previously sensitised → IgE antibodies against allergen → mast cell activation → massive mediator release (histamine, leukotrienes, prostaglandins, kinins)
 - Histamine leads to:
 - Smooth muscle contraction → bronchospasm
 - Vasodilation & ↑ permeability (can lose 1½ L of blood volume straight away)

- ↑HR and arrhythmias
- ↑Noradrenaline
- Itch & oedema
- Anaphylactoid reaction: activation of mast cells and release of mediators without IgE involvement.
Only relevant to investigating cause – not to treatment
- Examples of allergens:
 - Drugs: 50% of fatalities. Includes penicillin, muscle relaxants (can be sensitised by exposure to similar drugs), aspirin, contrast media, blood products, streptokinase, preservatives (e.g. in adrenaline)
 - Foods: 25% of fatalities. Peanuts, milk, eggs, fish
 - Insect bites: 25% of fatalities
 - Also latex, semen, blood products, physical stimuli (eg exercise, cold, heat)

Presentation

- Anaesthetics: If IV – then as fast as 1 minute, but normally 5 – 10 minutes. Food up to 30 minutes
- 1 in 2,500 surgical patients in Wellington. Death rate 4 – 6 %

Treatment

- Stop administration of antigen. Call 777
- Adrenaline:
 - If no current venous access then 0.5 ml 1:1000 IM. 0.01 mg/kg for kids
 - If venous access: 0.3 – 0.5 mls iv of 1:1,000 slowly, repeat until BP > 100. Start low (eg 10 µg) and titrate up
 - Can be nebulised for laryngeal oedema
 - If on TCAs then ↑sensitivity to adrenaline
 - α agonist → vasoconstriction – but not too much otherwise cardiac vasoconstriction
 - β agonist → bronchodilator
 - ↑Force of heart contraction
 - ↓Mediator release
 - T½ is short: common error is to give too little too infrequently
- Also:
 - Metaraminol (α agonist) to stop arrhythmias
 - ?Steroids: prevent late symptoms
 - Promethazine 25 mg slow iv or im (H1 antagonist) + H2 antagonist (e.g. ranitidine), or
 - Antihistamines: Phenergan 25 mg iv slowly for itch
- If bronchospasm alone:
 - Salbutamol: 5 – 20 µg/min
 - Hydrocortisone 200 mg iv
 - Aminophylline 5 mg/kg over 30 minutes
- Elevate legs → ↑venous return
- O2 10 l/min by mask: intubate if necessary
- Wide bore cannula → 1 – 2 l iv colloid rapidly
- If anaesthetic reaction, always investigate so next anaesthetic is safe. Should have skin tests, etc. Cross reactivity between muscle relaxants is not uncommon

Differential Diagnosis

- Measure serum **tryptase** (longer T½ than histamine) to confirm anaphylaxis
- Anaesthetic overdose: Tryptase raised in anaphylaxis, normal in overdose
- Respiratory: Pulmonary oedema/embolism, asthma, foreign body
- Heart: Pericardial tamponade, MI, arrhythmia, vasovagal faint
- Venous air embolism
- Septic shock
- Pneumothorax
- Transfusion reaction
- Hypoglycaemia, CVA, epilepsy

Prevention

- Avoid treatment with β-blockers – makes treatment of anaphylaxis difficult
- Carry and use adrenaline (eg Epi-pen)

- Medic alert bracelet
- Call an ambulance, don't 'wait and see'

Special Resuscitation Situations and Common Emergencies

Airway Obstruction

- Always consider in rapid cessation of breathing and unconsciousness. Also consider fainting, stroke, MI, epilepsy and drug overdose
- In adults especially related to meat, dentures and alcohol. Will grip throat not chest

Adult obstruction

- Partial obstruction → distressed and coughing. If conscious and adequate air → encourage coughing and spitting – nothing else
- Ask if they are choking: if can't talk, breath or cough then:
 - Remove obvious obstruction from mouth (only if unconscious – may bite). Grasp tongue and mandible between thumb and fingers and lift up. Hook with other hand
 - Back slapping: lean well forward onto one hand, 5 sharp slaps between shoulder blades with heel of other hand. If lying down, roll face down onto your thigh
 - Abdominal thrusts (Heimlich manoeuvre): fists over midline above naval, always below xiphoid process and ribs. Upwards thrust. May vomit. If on ground, lie on back and sit astride their thighs. If pregnant or obese, use chest thrusts
 - If obstruction is not relieved: check mouth, 5 back slaps, 5 abdominal thrusts, repeat

Paediatric Obstruction

- Suspect in any airway distress with coughing, gagging, or stridor with rapid onset. May also be caused by infections (e.g. croup or epiglottitis). If infective cause then medical emergency
- Only intervene if child's attempts to clear the obstruction are clearly ineffective and there is inadequate respiration
- For infants (<1 year) and children, 5 back blows with the child's head below the level of the chest if possible
- Then 5 chest thrusts to sternum in supine position: sharp, vigorous and rate of 20 bpm
- Check mouth: grasp tongue and jaw and lift. Don't put finger into mouth unless foreign body is clearly visible
- Reassess airway. If not breathing, attempt to ventilate
- Repeat back slaps, chest thrusts, attempted ventilation. In children, alternate abdominal and chest thrusts

Alcohol Withdrawal

- See Alcohol Withdrawal, page 452

Asthma

- Arrest due to: bronchospasm (→ asphyxia), tension pneumothorax (often bilateral), β agonists → arrhythmias
- Arrest Prevention:
 - Maximal O₂
 - Nebulised salbutamol (beware overdose → tachycardia and VF/VT) or iv 5 μ g/min up to 20 μ g if necessary
 - IV hydrocortisone
 - Adrenaline
 - IV sodium bicarbonate (acidosis prevents action of sympathomimetics)
 - Intubation and IPPV: sedate with ketamine or benzodiazepines, paralyse with suxamethonium
- During arrest:
 - Consider assisted exhalation (bilateral manual squeeze over lower chest at end of inspiration)
 - Plus normal routine
- See also Asthma, page 77

Burns

- Caused by: thermal, electricity, chemical, mechanical, radiation
- History:
 - Timing – start fluid maintenance calculations from time of injury not time of presentation
 - Circumstances – eg any risk of inhalational injury
 - Tetanus immunisation
- Classification:
 - Assessing depth:
 - 1st degree burns: Erythema (like bad sunburn)
 - 2nd degree: Blistering
 - 3rd degree: skin goes like leather
 - Now classified as:
 - Partial thickness burns (either 1st or 2nd degree): superficial heal in 2 – 3 weeks, deep need grafting
 - Full thickness burn
 - Body area covered: Rule of nines to estimate surface area burnt: head 9%, arms 9% each, thorax 18%, abdomen 18%, legs 18% each
- Admit if:
 - Major burn (>15% of adult, > 10% of child)
 - Special areas (hands, face, over joints, etc)
 - Circumferential – Require escharotomy to release pressure
 - Other medical conditions, etc
- Respiratory complications:
 - Upper airway burns: watch for oedema and obstruction. Prophylactic intubation if severe
 - Lower respiratory tract burns: Suspect if closed space fire, smoke inhalation or upper RT burns. Treatment: humidified O₂, PEEP, pulmonary toilet and physiotherapy. Avoid steroids
 - Inhalational injury a big killer – eg chemicals from burning materials → ARDS 24 hours later
- Watch for:
 - Hypovolaemia. See Replacement fluids, page 550 for fluid resuscitation
 - Good nutrition critical: ↑↑ calorie and protein requirements. Use NG tube
- For minor burns:
 - Analgesia
 - Wash gently
 - Dress with paraffin gauze and padding
 - Tetanus jab
 - Review in 3 – 4 days

Coma

- Immediate actions:
 - Establish unresponsiveness
 - Act as though cervical spine injury
 - Check ABC
 - If arrested → CPR
 - Consider ventilation/intubation
 - 100% O₂
 - IV access. Take blood for glucose, U&E, drug levels
 - Assess depth of coma: GCS
 - Expose and examine patient
 - Look for localising neurological signs, ↑intracranial pressure
 - Bladder catheterisation
- Further diagnostic options:
 - Chest, skull and cervical spin X ray
 - CT scan
 - Gastric lavage after protection of airway by intubation
- Consider:
 - Drugs/toxic (See also Poisoning and Overdose, page 488):
 - Alcohol: thiamine 100 mg iv
 - Opiod overdose: naloxone 0.4 mg iv

- Benzodiazepine overdose: flumazenil
- Also CO, fumes, antidepressants
- Metabolic: renal failure, endocrine (eg hypoglycaemia – Dextrose 25g iv), renal/hepatic encephalopathy, porphyria
- Miscellaneous: hypoxia, post epileptic fit
- Extracranial: hypoxia (due to arrest, asphyxia), hypo/hyperthermia, electrocution

Convulsions/Status Epilepticus

- See Status Epilepticus, page 135

Diabetic Ketoacidosis

- See Management of Diabetic Ketoacidosis or Hyperglycaemia, page 96

Electrolyte Abnormalities

- See Electrolytes, page 107. Includes Hyperkalaemia and Hypokalaemia

Electrocution

- Depending on shock, reasonable chance of survival from arrest
- Ensure your safety, start ventilation and compression ASAP
- Watch for airway if face, mouth or neck burns → swelling
- Rapid iv fluids if hypovolaemic shock or tissue destruction

Head Injury

- See Head Trauma, page 129

Hypertensive Crisis

- Signs: headache, vomiting, visual changes, convulsion, coma, angina, pulmonary oedema, CVA, eclampsia
- Treatment: sublingual captopril. Labetalol, etc
- Caution: vasodilators may increase ICP. May need iv fluids with vasodilators. Don't lower blood pressure too low too fast – cerebral autoregulation may be reset to a higher blood pressure

Near Drowning

- Effective immediate resuscitation critical. Use standard CPR procedure
- Remove foreign bodies from airways, don't attempt to drain fluid
- Suspect spinal injury if diving or in surf
- Early tracheal intubation may be indicated. 100% O₂
- Recovery may occur even after long immersion times, especially in cold water
- In hospital, cerebral oedema may require hyperventilation and diuretics
- Remember, alcohol or epilepsy may be involved
- Avoid steroids, consider antibiotics

Hypothermia

- Signs: hypotension, bradycardia, J wave on ECG, SV arrhythmias, VF at 28 C, metabolic acidosis, loss of consciousness at 28 – 30 C, shivering replaced by rigidity at 33 C, pupils dilated
- Lengthens tolerance of arrest: don't discontinue till they've been warmed
- Arrest prevention:
 - Prevent further heat loss
 - Transport avoiding rough movement, which can precipitate VF
 - If core temperature < 34 C, can rewarm with oesophageal rewarming tubes, peritoneal lavage (warmed saline or gas). Warm trunk not peripheries. Reduce movement (risk of VF). Rewarm slowly – 0.5 degrees/hour (unless fit and sudden hypothermia)
- During arrest:
 - Take 30 – 45 secs to confirm cessation of ventilation and pulselessness
 - Don't assume death until resuscitation has failed in an adequately rewarmed patient
 - If < 30 C give maximum of 3 shocks until core temperature increases
 - Reduced responsiveness to defibrillation and drugs. Impaired drug metabolism → watch for toxicity
 - Monitor fluids during rewarming

Hyperthermia

- Heat Exhaustion: hypovolaemic shock due to fluid loss through sweating. Cool, restore volume, position supine with legs raised
- Heat stroke: failure of heat regulation through failure to sweat. Hot, flushed and dry. If temperature > 40 degrees → neurological disturbances. Rapid cooling, cool iv fluids
- Reduces tolerance time for arrest
- Cooling can be external or internal
- Watch electrolytes and fluid replacement following arrest
- Watch for tendency to cerebral oedema and multi-organ failure

Poisoning and Overdose

- Cause of significant proportion of arrests in 18 – 35 year olds
- Duration of arrest and dose of toxin determinants of survival
- Do general management
- Manifestations of poisoning:
 - Exaggerated therapeutic response (eg sedation with BZD)
 - Pharmacological effects (eg respiratory depression, convulsions)
 - Accidental: children, single poison
 - Intentional: adult, often multiple, taken in conjunction with alcohol
- Management:
 - History:
 - Find out the drug if you can (has someone brought in the packet?): but only a few will change management (paracetamol, salicylates, lithium, paraquat, quinine, phenobarbitone, iron salts)
 - Very unreliable – especially the number of tablets taken
 - Supportive treatment:
 - A,B,C: Respiratory depression is the most common cause of death.
 - Maintain airway, check blood gases. Check for hypotension (→raise legs except in heart failure, volume expanders). Monitor electrolytes
 - Maintain safety: close supervision, no access to drugs on ward, etc
 - **Intensive support treatment:** IV fluids, ?NG tube, maintain vital functions, nursing care (eg suction, pressure sores, limb movement → ↓thrombosis)
 - **Treat complications:** hypothermia, hyperthermia (salicylates and stimulants – sponge down, use fan), seizures (iv diazepam), arrhythmias (leave bradycardia, tachycardia – correct acidosis, try amiodarone), hypoglycaemia (salicylates, oral hypoglycaemics)
 - Plus treatment specific to poison
 - Mental health assessment
- Investigations:
 - Blood levels: sometimes useful (eg Li, aspirin, theophylline, carbamazepine). Waste of time for TCAs
 - Urine Screen: Rarely changes management, no quantitative information, really only for criminal cases (eg after MVA)
- Corrosives:
 - *Never* induce vomiting
 - Drink copious fluids
 - Soak eyes, skin, mucous membranes
 - Petroleum: beware of inhalation, cup of milk
- Eliminating poisons. If sure it's not petroleum products, caustics, corrosives or acids, then options may include:
 - Activated charcoal
 - Better than emesis
 - Charcoal powder, mixed with H₂O: needs to be within 60 minutes. Give SINGLE 50 g dose in an adult (1 g/kg)
 - Reduces GI absorption of paracetamol, aspirin, phenytoin, digoxin, TCAs, theophylline, carbamazepine.
 - Don't use for volatile hydrocarbons or corrosives or an unprotected airway
 - Good for unionised drugs. Does not bind with acids, alkalis, alcohols, lithium.
 - Generally safe but constipation, aspiration may be problems (protect airway)

- Multiple doses only for drugs undergoing enterohepatic circulation or diffusing into the gut ⇒ drugs with a small Vd, low clearance, low protein binding and long T $\frac{1}{2}$. Eg Theophylline, carbamazepine, quinine, phenobarbitone. NOT Paracetamol.
- PH adjusted diuresis:
 - Alkaline diuresis: aspirin, phenobarbitone
 - Acid diuresis: amphetamine, methadone. Doubtful use and dangerous
- Dialysis: Haemodialysis. Only useful if low Vd, small molecule and low protein binding (eg lithium, theophylline, salicylates, alcohol and barbiturates)
- Whole bowel irrigation: ‘Go Lightly’ – Xray prep
- Questionable effectiveness:
 - Emesis: Not effective? Ipecac – never if airway reflexes not intact. Causes emesis in 90% within 15 – 30 minutes
 - Gastric lavage: large bore catheter through mouth. 1ml/kg of body temperature water, recover, repeat. Little evidence of benefit and ↑ risk of aspiration. Contraindicated if acid, alkali, or petroleum

Common poisons

- Paracetamol
 - Walk in, conscious
 - RUQ pain
 - Conjugation pathway easily saturated. Of the remainder, 15% is metabolised to a metabolite that combines with glutathione. If glutathione is depleted, metabolite causes hepatic damage
 - Toxic dose 140 mg/kg (textbook), 200 mg/kg (Starship), lower if chronic alcoholism, enzyme inducing drugs or fasting
 - Measure plasma concentration. Treat if > 200 µg/ml, 100 if liver disease, anorexia, etc. Threshold declines for each hour after ingestion
 - Absorbed quickly so gastric lavage or activated charcoal only effective within 45 minutes
 - N-acetylcysteine (NAC) best antidote – saturates alternative pathway so all the paracetamol is metabolised through the main pathway. Normal dose is 10 - 15 mg/kg per 4 hours acutely, per 6 hours at home
 - Monitor AST/ALT, PT (INR)
- TCAs: see Tricyclic Antidepressants, page 432
- MAOIs: see MAOIs (Monoamine Oxidase Inhibitors), page 434
- Opioids:
 - Marked sedation, pinpoint pupils, ↓↓ respiration (differential: stroke)
 - Naloxone (but short T $\frac{1}{2}$ → will lapse back)
- Stimulants (cocaine type drugs): ↑BP, tachycardia, arrhythmia, dilated pupils [sympathetic effects], seizures
- Barbiturates → flumazenil (can cause seizures – so not if SSRIs/TCAs/antihistamines as well – which also cause seizures)
- Dibenzazepine antidepressants: Rapidly absorbed, high Vd, protein bound. Look for myocardial toxicity, hypotension, hyperreflexia, convulsions. Treatment supportive + naso-gastric tube and charcoal (up to 24 hours later). Monitor ECG, iv propranolol and NaHCO₃
- Benzodiazepines: Diazepam, temazepam → Post –OD “cerebellar syndrome” (dizziness, confusion, ataxia, nystagmus, bullous lesions). Supportive treatment
- Anticonvulsants: carbamazepine
- Bronchodilators: theophylline
- Cocaine → benzodiazepines
- Carbon Monoxide → 100% oxygen, treat cerebral oedema. Presentation: pink, headache, vomiting, tachycardia, seizures, arrest
- Cyanide → 100% O₂ + cobalt edetate
- Methanol and ethylene glycol poisoning → correct acidosis, ethanol
- Chelating agents for arsenic, copper, lead, iron, cyanide
- Aspirin: risk is pH balance

Pulmonary Oedema

- Sit patient up and give O₂
- Medication:
 - IV frusemide: 40 – 80 mg if not on any already

- IV morphine: 5 – 10 mg – calming effect, ↓respiratory rate, venodilator → ↓preload
- Sublingual nitroglycerine
- If BP > 100 mmHg then captopril 6.25 mg
- Occasionally CPAP or IPPV
- Pulmonary oedema resulting from near drowning and ARDS does not respond to morphine & diuretics – may require ventilation

Renal failure

- Causes: ↑potassium, acidosis, uraemia, volume overload, toxic accumulation of drugs
- During arrest: give calcium chloride (to antagonise hyperkalaemia) + sodium bicarbonate

Spinal Shock

- Due to a shutdown of cord function (e.g. following trauma): may last several days
- IV fluids to maintain blood pressure: but don't overdo it. BP of 80/50 may be normal in spinal injury
- High dose methylprednisolone may be beneficial within 8 hours of spinal injury
- NG tube, urinary catheter (monitor output)
- Monitor ventilation, temperature, avoid pressure areas

Trauma to Abdomen

- Injuries may be blunt or penetrating
- Do a diagnostic peritoneal lavage (DPL) to look for bleeding
- A surgeon must evaluate all penetrating injuries of the abdomen.
- Intra abdominal visceral damage must be strongly suspected following blunt trauma to the abdomen. Multiple injuries are common and signs and symptoms guide diagnosis. Note that distracting injuries (eg fractures) may mask abdominal symptoms.

Indications for surgery

- Unstable patient
- Injury penetrates peritoneum
- Significant pancreatic injury on CT
- Significant splenic injury in an older patient
- Arterial injury

Specific Injuries

- Ruptured spleen (intraperitoneal haemorrhage)
 - Signs and symptoms: May be pain free, may have signs of blood loss
 - Treatment: Splenectomy if elderly otherwise try to preserve it
- Ruptured liver: Treatment: Laparotomy and suturing individual vessels/ packing etc.
- Ruptured gut: Presence of gas under diaphragm on x-ray, or history of penetrating wound needs laparotomy and repair/resection of affected bowel

Trauma to Chest

Tension Pneumothorax

- Signs:
 - Apex beat lost
 - Blocks IVC → ↓venous return → ↑JVP
 - ↓Vocal fremitus
 - Hyper-resonance
 - Displaced trachea (maybe)
 - US may help with diagnosis
- On X-ray must have *both* of no peripheral vascular markings *and* a visceral pleural line
- Types:
 - Primary/spontaneous: apical sub-pleural blebs are common and occasionally rupture. Especially tall, thin, young males. Can occur at rest. Recurrence 20%
 - Secondary: in any lung disease
- Treatment:
 - Insert 14g iv cannula into midaxillary line at level of nipple (any lower and may get diaphragm)
 - Hissing of air is diagnostic

- Remove needle and leave cannula in place. Attach tubing and put other end under water
- PP ventilation will help reinflate the lung
- Insertion where there wasn't a pneumothorax will cause one!

Open Pneumothorax

- Sucking wound \Rightarrow can't create -ive intrathoracic pressure
- Occlusive dressing and positive pressure

Massive Haemothorax

- 1500 ml in thorax or > 200 ml per hour
- Mainly penetrating wounds of pulmonary vessels (e.g. intercostals). If great vessels affected usually don't survive
- Significant amount of blood needs surgical removal \rightarrow thoracotomy

Flail Chest

- Needs lots of force – so suspect pulmonary contusion as well
- Independent segment of chest wall \rightarrow paradoxical movement. Requires two breaks
- Treat with IPPV for at least a week

Cardiac Tamponade

- Commonly results from penetrating injury
- Commonly confused with a pneumothorax – think pneumo-thorax first – more common
- Signs:
 - Impaired diastolic filling $\rightarrow \downarrow$ stroke volume. Initially tachycardia and vasoconstriction maintain cardiac output and BP. Eventually hypotension and shock
 - Cardinal signs: Beck's triad – hypotension, \uparrow venous pressure (\uparrow JVP), small quiet heart
 - Pulsus paradoxus: > 10 mmHg \downarrow in systolic BP with normal inspiration
- Treatment:
 - Emergency pericardiocentesis (either via xyphisternum or into apical area). Surgery essential
 - Colloid fluid infusion $\rightarrow \uparrow$ filling pressure and stroke volume

Pulmonary Contusion

- Leads to non-compliance: V/Q mismatch, shunting $\rightarrow \downarrow$ PO₂
- Ventilate

Myocardial Contusion

- Suspect if fractured sternum (requires big force)
- There will be a current of injury on ECF and cardiac enzymes
- Causes arrhythmias and \downarrow CO
- Treatment: 24 hours observation under ECG – can be arrhythmias

Rib Fracture

- Commonest injury: pain impairs ventilation
- Complications: atelectasis, pneumonia, contusion, pneumothorax, secondary pleural effusion 2 – 3 weeks later
- Treatment: pain relief

Traumatic Rupture of Aorta

- Results from rapid deceleration, usually at ligamentum arteriosum
- Immediately fatal in 90% of cases. 50% further mortality per 24 hours thereafter untreated
- Diagnosis suspected on CXR: widened mediastinum, 1st & 2nd rib fracture, obliteration of aortic knob, deviation of trachea. Definitive diagnosis by aortogram
- Treatment: repair
- Complications: paraplegia due to \downarrow blood flow to spine

Infectious Diseases

- References: Predominantly drawn from Dr M Humble's Microbiology notes
- For notifiable diseases, see Communicable Disease Control, page 686
- For infectious diseases of the skin, see Skin Infections, page 315
- For infectious diseases in children, see Infectious Diseases, page 616
- For respiratory infections, see Acute Pharyngitis, page 63 and Adult Pneumonia, page 67
- For urinary tract infections, see Urinary Tract Infections, page 219
- For gastro-intestinal infections, see Diarrhoea – Infectious Agents, page 176 and Viral Hepatitis, page 186

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Blood Culture

- When to take them:
 - It takes 30 – 60 minutes for temperature to rise after introduction of bugs into the blood, but endothelial cells of the vascular system (spleen, kuppfer cells, etc) phagocytose cells in minutes
 - So when the temperature spikes, bugs may well be gone. So do *random* cultures in the hope of getting a hit
- Definitions:
 - Bacteraemia: no host response. Happens all the time (eg after cleaning teeth)
 - Septicaemia: sustained bacteria in the blood stream – on going delivery of bugs into the blood stream from a replicating focus (don't multiply in blood). Leads to host response and disseminated loci of infection
 - Pyemia (older term): Spread of organisms via infected thrombi
- Infections associated with bacteraemia:
 - Community acquired pneumonia (treat strep pneumonia with penicillin, except in children where > 30% resistance so use cephalosporin)
 - Meningitis with petechial rash (treat meningitidis with penicillin)
 - Osteomyelitis (treat S Aureus with flucloxacillin or vancomycin if MRSA)
 - Leukaemia with infected Hickman line (Coag –ive staph, eg epidermidis, treat with vancomycin)
 - Pyelonephritis (treat E coli with Gentamycin)
 - Cellulitis (treat Strep pyogenes with Penicillin)
 - Perforated appendicitis (treat B Fragilis with Metronidazole)
 - Infective endocarditis (treat viridans Strep, eg S sanguis, with penicillin + maybe gentamycin)
 - Epiglottitis (treat HIB with cephalosporin)
 - Premature baby with respiratory distress syndrome (treat Lancefield group B strep with penicillin)
- Procedure for blood culture:
 - Ensure everything sterile – contamination makes interpretation very difficult
 - 5 – 10 mls of blood in two bottles, one general purpose and the other anaerobic
 - For kids, use single 3 ml paediatric bottle
 - Choose vein (usually ante-cubital fossa)
 - Swab with betadine and wait 3 – 4 minutes to dry
 - Draw blood and inject into bottles
 - If already on antibiotics, notify lab
- Indications for blood cultures:
 - Infection of any degree of severity – especially if firm clinical diagnosis not possible
 - Absence of fever doesn't rule out infection, so is not a contra-indication (eg confusion, feeling off)
 - Specific indications:
 - Acute generalised infection: fever, rigors, sweating, shock
 - Febrile illness + congenital or acquired heart disease where infective endocarditis suspected
 - Diseases with a bacteraemic phase (pneumonia, meningitis, acute pyelonephritis, etc)
 - Shock (especially post-operative following abdominal surgery)
 - Intercurrent illness in patients with compromised immunity
 - Usually unnecessary to do more than 2 sets at the time bacteraemia is suspected, 20 minutes apart. If infective endocarditis, take 3 sets over 24 hours
- Bugs isolated in Wgtn Hospital:
 - Four most common G+ive: Staph aureus, Staph coag –ive (from lines), strep pneumonia, enterococcus faecalis
 - Four most common G-ive: E. Coli, Klebsiella, Other Coliforms, Pseudomonas aeruginosa
 - Most common is staph epidermidis (ie staph coag –ive): It's a common contaminant, but also the most common pathogen in catheter related infections, neonates and neutropenic patients.
↑Resistance to Flucloxacillin → ↑use of vancomycin (expensive, side effects, etc)

Infections of the CNS

Bacterial Meningitis

Signs and Symptoms

- Rapid onset of:
 - Meningism: Headaches, photophobia, stiff neck. Kernig's sign: Pain on straightening knee with hip flexed
 - ↑ICP: Headache, irritable, drowsy, vomiting, fits, ↓pulse, ↑↓BP, ↓LOC, pin-point pupils, papilloedema (late sign), tense fontanelle
 - Septicaemia: fever, arthritis, DIC, ↓BP, ↑pulse, tachycardia, rash (ultimately 80% will have a purpuric rash, 10 – 15% will have a maculo-papular or urticarial rash, 5 – 10% will have no rash)
- In different age groups:
 - Infants/toddlers: fever, lethargy, poor feeding, vomiting, toxic (drowsy, pallor), rash. Only 30 – 50% have signs of meningism ⇒ absence doesn't exclude. Bulging anterior fontanelle – but if vomiting may be normal or reduced
 - Children > 3: fever, headache, vomiting, photophobia, stiff neck, confusion (may be combative), non-blanching rash (initially blotchy macular rash that rapidly becomes petechial or purpuric)
 - Adolescents: may present as acute mania or appearance of drug induced psychosis

Pathogenesis

- Organisms:
 - Neonates: E. Coli, β-haemolytic streptococci Group B (eg streptococcus agalactiae – normal vaginal flora), rarely listeria
 - Children < 14 years: H. Influenza (if < 4 and not immunised), Neisseria Meningitidis Type B, Strep Pneumoniae, Tb
 - Adults: Neisseria Meningitidis Type B, Strep Pneumoniae, maybe staph aureus or Cryptococcus neoformans
 - Elderly, Immunocompromised: Pneumococcal, Listeria, Tb, G –ive, Cryptococcus Neoformans
- Pathogenesis:
 - Pathology: inflammation of pia mater and arachnoid
 - Most common are N Meningitidis and S pneumoniae
 - Nasopharynx → blood → subarachnoid space (via choroid plexus): N meningitidis, HIB, S. pneumoniae
 - Middle ear → blood → subarachnoid space: S Pneumoniae, HIB
 - Congenital abnormalities (eg spina bifida): coliform bacilli, pseudomonas, Strep agalactiae
 - Trauma: Skull fracture + CSF leak, CNS surgery, shunts: Staph aureus
 - Depressed immunity: listeria monocytogenes, cryptococcus neoformans
 - Neonatal meningitis from vaginal flora (especially with prematurity, prolonged ROM, delayed 2nd stage): Strep agalactiae, coliforms (E coli), listeria monocytogenes
- If recurrent:
 - Consider immunosuppression (eg hypogammaglobulinaemia or complement deficiency)
 - Look for lumbosacral defects, especially if enteric bacteria or S aureus

Investigations

- Do blood culture before presumptive treatment if possible, but NOTHING should delay presumptive treatment. Tell lab about antibiotics
- Must do:
 - Blood cultures
 - CSF via lumbar puncture unless contraindicated (see below)
 - Urine: supra-pubic aspiration or catheter
 - If antibiotics have already been administered:
 - Needle aspirate purpuric lesions for gram stain and culture
 - Throat swab
- Bloods:
 - Blood Glucose sample – may be hypoglycaemic [ABC = Airway, breathing, circulation. DEFG = Don't Ever Forget Glucose]
 - FBC, electrolytes, clotting time, ABGs

- Lumbar puncture:
 - Contraindicated if:
 - Signs of ↑ICP* (all meningitis will have ↑ICP) causing cerebral herniation (eg very ↓LOC, very bad headache, focal signs including abnormal papillary reflexes, tonic seizures, decerebrate or decorticate posturing, irregular respirations, bradycardia, papilloedema). If in doubt then CT
 - Severe cardiovascular compromise with DIC/coagulopathy (eg fulminant sepsis)
 - Infection over the injection site
 - Tests of CSF: Gram stain, Tb, cytology, virology, glucose, protein, India ink (Cryptococcus), culture (if clear then ?virus), antigen testing (especially if partially treated)
 - May be normal, repeat if symptoms persist
 - Typical CSF (lots of variation):

Main cell seen	Pyogenic	Tb/Fungal	Viral ('aseptic')	Normal
Polymorphs		Mononuclear	Mononuclear	< 5 * 10E6 WBC/ml (< 20 in neonates)
Glucose	↓↓	↓	- or ↓	2.5 – 5.0 mmol/l
Protein	↑↑	↑	Mildly ↑ or ↓	< 0.4 g/l
Bugs seen	Yes	No	No	

 - NB: early viral meningitis may have predominantly polymorphs
 - RBCs: None. If there are then either traumatic (more in 1st of 3 tubes) or bleed (new if red, yellow if old – zathachromia)
- Appearance on Gram stain:
 - N Meningitidis: G –ive diplococci
 - H influenzae: Pleomorphic G –ive bacilli
 - S pneumoniae & S agalactiae: G +ive diplococci
 - Listeria: G +ive bacilli
 - TB: Acid fast bacilli very scant – take at least 5 mls of CSF
 - Cryptococcus neoformans: Indian ink stain shows capsules
- Imaging: To identify subdural collections, abscess, hydrocephalus, thrombosis and infarction. Only if LP contraindicated and suspected mass lesion or persistent or focal neuro signs

Management

- See When is a child really sick?, page 565
- Management (based on protocol for a child):
 - Standard infection control precautions plus surgical mask when examining throat, intubating etc
 - ICU if:
 - Coma
 - Circulatory collapse
 - Persistent, recurrent seizures
 - SIADH with cerebral oedema or seizures
 - Shock or ↑ICP is what kills
 - Maintain perfusion:
 - Colloid bolus (20 – 40 ml/kg 4% albumen iv), then colloid + glucose
 - Inotrope eg dobutamine (10 µg/kg/min)
 - Watch for ↑ ADH secretion → hyponatraemia and cerebral oedema if too much fluid given
 - Check Na 6 – 12 hourly. If Na < 135 mmol/l then ↓iv rate. If Na > 145 then ↑rate
 - Respiratory support:
 - O₂
 - Early elective intubation if persistent shock (but may exacerbate hypotension due to vasodilation and ↓sympathetic drive)
 - Immediate intubation if ↑ICP, hypoxia and/or respiratory failure, pulmonary oedema or hypotension (uncompensated shock)
 - Correct abnormalities: anaemia, hypoglycaemia, coagulopathy (FFP), acidosis (NaHCO₃), hypokalaemia
 - Seizures: anticonvulsants
 - Watch for ↑ICP:
 - ↓Conscious state, focal neuro signs, abnormal pupils, hypertension and relative bradycardia.

- Treatment: ICU, ↓PCO₂, diuretics (Mannitol, frusemide), head up, deep sedation, inotropes.
But priority is to correct the shock (CBF = MAP – ICP)
- Weight and measure head daily in an infant
- Isolate patient, ensure analgesia
- Dexamethasone treatment controversial (most benefit in HIB). Not routinely used. Reduces fever and gives misleading impression of clinical improvement
- **Antibiotic regimes:**
 - Empiric antibiotic treatment:
 - Neonate – 3 mths: Amoxycillin 50 mg/kg (for listeria) + Ceftriaxone 50 mg/kg (E coli and Strep). 2 weeks for G +ive, 3 weeks for G -ive.
 - Older child:
 - Cefotaxime 50 mg/kg/6hr, max 2 g, iv for 7 – 10 days or
 - Ceftriaxone 50 mg/kg/12hr, max 2 g, iv for 7 – 10 days or
 - Penicillin G 50 mg/kg/4hr iv for 7 – 10 days
 - If strep pneumonia suspected: *Vancomycin 15 mg/kg/6hr, max 500 mg, iv + cefotaxime/ceftriaxone* – synergistic, necessary due to ↑resistance to 3rd generation cephalosporins
 - If still failing consider adding Rifampicin
 - Specific Treatment according to culture and susceptibility results:
 - N Meningitidis, S agalactiae: Penicillin (Cefotaxime if allergic to penicillin) for 5-7 days. For meningococcaemia only can use penicillin or cefotaxime
 - S pneumoniae:
 - Penicillin susceptible: penicillin (but 20% are resistant) for 7 – 10 days
 - Penicillin resistant, 3rd generation susceptible: Cefotaxime
 - Penicillin and 3rd generation resistant: Cefotaxime + Vancomycin
 - H Influenza: Cefotaxime, Ceftriaxone
 - L Monocytogenes: amoxycillin
 - Staph Aureus: Flucloxacillin
 - M Tuberculosis: Rifampicin, Isoniazid, Pyrazinamide, Ethambutol
 - Coliforms: 3rd generation Cephalosporin (ie Cefotaxime, Ceftazidime)
 - Pseudomonas: Ceftazidime
 - Cryptococcus Neoformans: fluconazole or amphotericin B
 - NB: Erythromycin and gentamycin don't have good CSF penetration
 - If not responding, or non-susceptible strain of pneumococci or receiving dexamethasone than repeat LP after 24 – 48 hours
- Complications:
 - Seizures:
 - First suspicion should be hyponatraemia (also hypoglycaemia):
 - SIADH (Na < 130 and urine Na > 20) → exacerbates cerebral oedema
 - Prevent by restricting fluids to 50% of maintenance
 - Treatment: severe fluid restriction (10 ml/kg/day), in an emergency consider hypertonic saline, Mannitol or frusemide
 - Hypoventilation can further ↑ ICP → hypoxia, hypercapnea, acidosis
 - Anticonvulsants can also exacerbate these metabolic changes
 - Management options: diazepam, clonazepam, phenobarbitone, dextrose to control hypoglycaemia, intubation and ventilation
 - Major disability in 15%: *Deafness*, brain damage, peripheral necrosis, etc. All cases should have audiologist check within 6 – 8 weeks of discharge
 - Death in 5%, 10 – 15% pneumococcal meningitis, 20% in fulminant meningococcaemia

Meningococcal Disease

- Cause: Neisseria Meningitidis
- Epidemiology:
 - 10-year epidemic started in 1990 with about 50 reported cases. Since then 3696 cases and 163 deaths. Current case fatality rate is 3 – 5 %
 - Leading infectious cause of death in children
 - 500 reported cases in 2000. NZ rate is 13.3 per 100,000. UK rate is 4 per 100,000
 - Regional variation: East Cape and Central North Island the highest
 - Rates per 100,000 < 1 year olds:

- Pacific Island: 570
- Maori: 230
- European: 80
- Healthy people can be carriers
- Transfer via respiratory secretions
- Kids and teenagers more susceptible than adults
- Not a cause of Otitis media
- Pathogenesis: endotoxins (lipopolysaccharides in the cell wall) activate complement and release of PAF causing endothelial injury → immune activation and ↑vascular permeability
- Notifiable to public health (as is HIB)
- Prophylaxis to stop nasal carriage of the bug – not to cure incubating illness. Nasal carriage higher in adults than children
 - Rifampicin: 4 doses, 600 mg bd for adults, 10 mg/kg bd for kids (very high dose). Broad spectrum antibiotic
 - Offer to index case (if only treated with penicillin), all intimate, household and day-care contacts during last 10 days
 - Contraindications: pregnancy (use single dose ceftriaxone), liver disease.
 - Side effects: nausea, vomiting, diarrhoea (GI effects), turns urine/tears/sweat orange/red (will stain contacts)
 - Interactions: asthma, blood clotting and oral contraceptives (continue pill, use barrier method until 7 days after antibiotics finished)

TB Meningitis

- Rare
- Most common < 5 years
- Slow onset: malaise and fever progressing to drowsiness, neck stiffness and seizures over 2 weeks
- Mantoux testing may be normal, and CXR normal in ½ of cases
- Investigations:
 - Gastric lavage, urine and CSF for Acid fast stain and culture
 - CT
- Treatment: isoniazid, rifampicin, pyrazinamide
- Notifiable disease

Brain Abscess

- Aetiology:
 - Chronic otitis media, sinusitis or dental sepsis
 - Trauma: foreign body, skull fracture, CNS surgery
 - Haematogenous spread (may be multiple abscess) from congenital heart disease (with R-L shunt), bronchiectasis, abdominal abscess, endocarditis, etc
- Bacteria:
 - Temporal lobe (from chronic otitis media):
 - Anaerobes: Bacteroides fragilis
 - Aerobes: Proteus mirabilis + HIB and E faecalis
 - Frontal lobe (from chronic sinusitis)
 - Anaerobes: Bacteroides melaninogenicus
 - Aerobes: Strep milleri
 - Traumatic: Staph aureus
 - Haematogenous spread: Staph aureus, Viridans Strep, Bacteroides fragilis, etc
- Treatment:
 - Surgery
 - Antibiotics:
 - Anaerobes: Metronidazole
 - Aerobes:
 - Strep: Amoxycillin
 - Coliforms: Cefotaxime
 - Staph aureus: Flucloxacillin

Viral CNS Infections

Viral Encephalitis

- Herpes Simplex:
 - Clinical: usually short history, fever, headache, confusion, ataxia, focal convulsions → coma (if clouding of consciousness consider encephalitis in addition to meningitis)
 - CSF: raised leucocyte count, predominantly mononuclear
 - Diagnosis: PCR test of CSF for Herpes Simplex antigen
 - Treatment: Acyclovir 10 mg/kg iv 8 hourly for 10 days. Low threshold for treatment
- HIV:
 - Most AIDS patients have a subacute encephalitis caused by direct brain infection
 - Symptoms: mood changes, depression, lethargy, confusion, dementia
- Other viruses: Mosquito born (Murray Valley Encephalitis, Japanese Encephalitis), Rabies virus
- Management:
 - Full blood screen: Cr, electrolytes, glucose, LFT, ABG, urine drug & metabolic screen, blood and urine cultures, ammonia, cortisol, coagulation screen, ECG
 - Serology and viral cultures
 - LP if not contraindicated – may be normal in up to 50% of cases
 - Consider empiric acyclovir + cefotaxime – at least until HSV is excluded
 - CT (MRI better still) for focal lesions
- Consider differential:
 - Head injury
 - Toxic or metabolic encephalopathy
 - Hypoxic insult
- Supportive treatment:
 - Fluid restriction
 - Control of seizures
 - Cardio-respiratory support
 - Maintenance of nutrition

Viral Meningitis

- Causes:
 - Most due to non-polio enteroviruses:
 - Faecal → oral ⇒ little kids at risk
 - ECHO viruses, Polio, Coxsackie A & B
 - Mumps
- Presentation: fever, headache, malaise, photophobia, abdominal pain and vomiting. Neck stiffness in older children. Maybe a macular or even petechial rash
- Differential diagnosis of lymphocytic (aseptic) meningitis
 - Viral meningitis (eg ECHO, Mumps, Coxsackie)
 - Viral Encephalitis (eg Herpes Simplex, CMV, Varicella Zoster)
 - TB meningitis
 - Fungal meningitis (eg Cryptococcus neoformans)
 - Neurosyphilis
 - Acute Leptospirosis
 - Cerebral toxoplasmosis
 - Neoplasm
 - Cerebral sarcoid
- Lab tests:
 - CSF Culture: Enteroviruses, mumps, fungi, TB
 - Throat culture and Faeces for enteroviruses
 - CSF Antigen tests: PCR for Herpes Simplex, CMV, VZV, TB, Toxoplasmosis
 - Serology: antibodies to Treponema pallidum, Leptospira, Toxoplasma gondii
- Admit if:
 - Diagnosis in doubt
 - Antibiotics are being considered
 - IV Rehydration is needed
- Ensure good analgesia

Post-Infective Encephalitis

- Immune hypersensitivity reaction to host cells containing viral antigens
- Late onset – 7 – 10 days after acute illness
- Viruses involved: Morbilli (Measles), Mumps, Rubella, Varicella-Zoster

Other

- Spongiform encephalopathies:
 - Caused by Prions (Proteinaceous infectious particles)
 - Histology: vacuolation of brain tissue, deposition of amyloid plaques
 - Eg: Kuru (in PNG), Creutzfeldt-Jakob Disease (CJD), Variant CJD
 - Symptoms: Insidious onset of ataxia, dysarthria and dysphagia. Progressive dementia
 - See Dementia, page 439
- Slow virus infections:
 - SSPE (Subacute sclerosing pan-encephalitis): Measles like virus affecting children and adolescents
 - PML (Progressive Multifocal Leucoencephalopathy): Affects adults from 40 – 70, Polyoma virus implicated.
- Neonatal Encephalitis:
 - TORCH Complex: Toxoplasmosis, Rubella, CMV, Herpes Simplex
 - Usually accompanied by disseminated disease
- Reye's Syndrome: post-infectious encephalopathy with associated acute liver failure. Most common antecedent infection is Influenza virus

Bacterial Disease

Streptococcus

Streptococcus Pyogenes (Group A, β Haemolytic)

- NB: Lancefield Groups only apply to β Haemolytic Strep
- Causes:
 - Commonly: acute pharyngitis, cellulitis, impetigo (also caused by group C)
 - Uncommonly: necrotising fasciitis (haemolytic strep gangrene), strep toxic shock syndrome, scarlet fever, erysipelas (= contagious skin infection with strep pyogenes), acute otitis media
 - Rarely: pneumonia, infective endocarditis
- Has remained sensitive to penicillin
- Identical strep can lead to a variety of infections:
 - Sore throat
 - Impetigo/Cellulitis. See Impetigo (School Sores), page 315
 - Toxic Shock Syndrome
 - Myositis
 - Necrotising Fasciitis
- Infection via throat (mainly) or via skin (impetigo/wound infection):
 - Suppurative: tissue invasion
 - Non-suppurative (after 2 – 8 weeks):
 - Rheumatic Fever (See Rheumatic Fever, page 602)
 - Glomerulonephritis
 - Super antigens: pyrogenic exotoxins – ability to avoid classical antigen processing by APCs
- **Scarlet Fever:**
 - Direct response to Streptococcal toxins (cf virus rash which is autoimmune and therefore delayed)
 - Presentation: fever, exudative pharyngitis, scarlatina rash (fine punctate rash with perioral sparing), desquamation
 - Skin feels like sandpaper then desquamates. May get purpura in flexures
 - Tongue affected – white then strawberry red
- **Streptococcus Toxic Shock Syndrome:**
 - First described in children. Now associated with Tampon use
 - Early (1 – 7 days): vague, viral like illness: fever, chills, myalgia, diarrhoea
 - Later: abrupt onset of pain (not necessarily associated with findings), redness, hypotension, renal failure, ARDS, coagulopathy. May lead to necrotising fasciitis. Also skin diffusely erythematous like sunburn, conjunctivitis

- Desquamation a week later characteristic
- Age group: 2- 50 year olds, no predisposing or underlying disease
- Bacteriology:
 - Blood culture +ive in 60%
 - Swab or aspirate in 95%
 - M protein types 1 & 3: impedes phagocytosis by leucocytes, expressed on cell wall
- Lab tests: Haematuria, ↑Cr, ↓albumin and ↓Ca, serum CK for deep tissue infections
- Treatment: Ceftriaxone
- **Necrotising fasciitis:**
 - Diffuse swelling and mild erythema, followed by bullae filled with clear fluid. Spreads along facial planes
 - Infection of subcutaneous tissue → progressive destruction of fascia and fat but may spare the skin itself.
 - 25 cases per year in NZ
 - Requires aggressive surgical debridement
 - Causative bacteria:
 - Group A strep most common
 - Staph Aureus
 - C. Perfringens
 - C. Sceptica
 - Predisposing factors:
 - Diabetes
 - Peripheral vascular disease
 - Chicken pox
 - Minor trauma/surgical procedures
 - Use of NSAIDs masks inflammation and delays diagnosis

Streptococcus Lancefield Group B

- β Haemolytic Streps
- Eg Strep agalactiae: differential in neonatal meningitis. Normal vaginal commensal

Streptococcus Pneumoniae

- Is α haemolytic but not classified as a Viridians
- Causes:
 - Commonly: acute otitis media, acute sinusitis, febrile convulsion in infants, community acquired pneumonia, infectious exacerbations of chronic bronchitis, meningitis (nasty type)
 - Uncommonly: peritonitis (2ndary to chronic hepatic/renal disease or to infected IUD)
 - Rarely: infective endocarditis
- Antibiotic sensitivity:
 - Parenteral:
 - Penicillin resistance in 1% blood isolates in adults and 11% in kids ⇒ Strep pneumonia penicillin resistance is not an issue in adults but is in kids
 - Ceftriaxone
 - Vancomycin (for penicillin resistant strains and MRSA)
 - Oral: amoxycillin, erythromycin, cefaclor, tetracycline (not kids or pregnant)
- Vaccination:
 - Pneumovax
 - Polysaccharide-based subunit vaccine containing 23 serotypes covering 90% of strains causing invasive pneumococcal disease
 - Contains T-cell independent antigens ⇒ non-immunogenic if < 2 years (and poor response for some serogroups up to age 6). Predominant IgM response without induction of memory. 5 yearly boosters recommended
 - Recommended for:
 - > 65 years
 - > 2 with asplenia, immunocompromised (including nephrotic syndrome) and chronic illness
 - Conjugate vaccines generating IgG response being worked on....

Viridians Streptococci (plus also Enterococcus faecalis)

- Causes UTI, abdominal wound sepsis, infective endocarditis (uncommon)

Staphlococcus

Staphlococcus Aureus

- Sources of bacteraemia:
 - Skin sepsis
 - Wound infection (esp hospital acquired)
 - Pneumonia (esp hospital acquired)
 - Osteomyelitis
 - Septic arthritis
 - Lines: Subclavian, IV drips (esp CVP)
 - Infective endocarditis
- See also Impetigo (School Sores), page 315

Staphlococcus coagulase negative (eg epidermidis)

- Sources of bacteraemia: IV lines – Hickman, CVP lines, premature neonates with IV lines

Haemophilus Influenzae

- Uncapsulated type (not type B which is capsulated)
- Causes:
 - Commonly: acute otitis media, acute sinusitis, acute infectious exacerbation of chronic bronchitis
 - Uncommonly: community acquired pneumonia (more CORD patients)
 - Rarely: meningitis
- Antibiotic sensitivity:
 - 5% of isolates produce penicillinase \Rightarrow resistant to amoxycillin
 - Augmentin
 - Cefaclor
 - Tetracycline (not kids or pregnant)
 - Cefuroxime (iv)
 - Is not sensitive to erythromycin

Moraxella Catarrhalis

- Previously known as Branhamella Catarrhalis
- Commonly causes: acute otitis media, acute sinusitis, acute infectious exacerbation of chronic bronchitis (same as Haemophilus Influenzae)
- Antibiotic sensitivity: 70% produce penicillinase, so use augmentin, cefaclor, tetracycline or cefuroxime (iv)

Other G-ives

- Escherichia coli, klebsiella aerogenes, proteus mirabilis, other Coliform bacilli
- Cause: UTI, Pyelonephritis, abdominal wound sepsis, peritonitis, biliary tract infection (gallstones) or obstruction

Anaerobes

- Bacteroides fragilis, Clostridium perfringens, anaerobic streptococci
- Cause: Abdominal wound sepsis, peritonitis, pelvic sepsis, septic abortion, puerperal sepsis

Mycobacteria

- See Tuberculosis, page 68
- Classification:
 - Tuberculosis complex: M. Tuberculosis and M. Bovis
 - Other mycobacteria: M. Avium-Intracellulare (MAC), M. Kansasii, M. Marium
 - Leprosy: M. Leprae
- Resulting Diseases:
 - Tuberculosis Complex
 - Immunocompetent: In descending frequency: lung, lymph nodes, kidney, genital tract, CNS
 - Immunodeficient: Lung in > 70%, but extra pulmonary involvement > 70% in blood (25 – 40%), lymph nodes, faeces, CNS due to ↓cell mediated immunity
 - MAC:

- Immunocompetent: Kids – cervical lymphadenitis, adults: chronic destructive lung disease (uncommon)
- Immunodeficient: Infection common. Initial colonisation of GI tract, then spread to blood, lymph nodes, liver, spleen, less lung involvement but invariably fatal
- Most strains of MAC are resistant to standard anti-mycobacterial drugs
- Drug treatment:
 - Standard drugs: Rifampicin, Isoniazid, pyrazinamide, ethambutol. Normally first 3, except if from Pacific Islands where use all 4 due to ↑isoniazid resistance. Rifampicin is the best, if resistant to this then poor prognosis
 - Most strains of M Bovis are resistant to pyrazinamide
 - Many strains of M Tb from AIDS patients in the US (especially NY) are resistant to Rifampicin and Isoniazid
 - Other anti-mycobacterial drugs: ciprofloxacin, clarithromycin, amikacin, rifabutin, clofazimine
- Vaccination: BCG:
 - Live vaccine
 - Indicated for high risk infants: household has individuals from endemic areas or with past or current Tb
 - Neonatal BCG is 60 – 90% protective for extra-pulmonary Tb and 65% for pulmonary Tb. Protection lasts 10 – 15 years
 - Adverse effects: local abscess in 1%. Treated conservatively. Some require excision

Herpes Viruses

- All Herpes viruses exhibit latency

Herpes Simplex Virus (HSV)

- Manifestations: systemic (fever, sore throat), gingivostomatitis (ulcers with yellow slough – cold sores), meningitis (uncommon, self-limiting), encephalitis (fever, fits, headache, dysphagia, hemiparesis – do PCR on CSF sample – refer urgently)
- Incubation: 2 – 25 days. Chronic infection is due to the virus remaining in the sensory nerve ganglia. Infectious period indeterminate → contact isolation
- Symptoms:
 - Blisters which become shallow painful ulcers, often preceded by itching or tingling
 - First episode may be accompanied by flu like illness, tender inguinal nodes and dysuria
 - Recurrences can be brought on by stress, fatigue, depression, immunosuppression and concurrent illness. Recurrences usually less severe and become less frequent
- Diagnosis: clinical suspicion. Swab the base of an unroofed ulcer and refrigerate in viral medium. This will be painful. Culture negative doesn't exclude HSV as timing and collection technique important. Serology possible, but not routinely used
- Pathogenesis. There are two antigenic types of Herpes Simplex Virus:
 - Type 1 is associated with lesions on the face and fingers, and sometimes genital lesions. Treat with zovirax (topical cream). Prevalence: 70% of population
 - Type 2 is associated almost entirely with genital infections, and affects the genitalia, vagina, and cervix and may predispose to cervical dysplasia. 10% of oral lesions caused by type 2. Prevalence: 10 – 15% of population (depends on population – more in high risk)

Type 1 Herpes Simplex Virus

- Infection of fingers or thumb leads to a whitlow (vesicles coalesce)
- Can infect eczematous skin → eczema herpeticum
- Children:
 - HSV1 the most common type in children.
 - Primary infection in childhood leads to gingivostomatitis – may lead to dehydration as child won't drink. May need NG tube
 - Dribbling can → perioral spread
 - Auto-inoculation can → conjunctivitis, genital lesions, skin infection with eczema (eczema herpeticum) can be severe
 - If neonate or immunocompromised can be life-threatening
 - Treatment: Oral analgesics (eg lignocaine) and Paracetamol. Acyclovir

Genital Herpes (type 2)

- Description:
 - Painful, recurrent condition.
 - Male – anus or penis – small grouped vesicles and papules + pain, fever, dysuria. Dysuria may be severe enough to cause urinary retention
 - 20% may have it, but 20% are asymptomatic and 60% mild or unrecognised
- 40% caused by type 1, 60% by type 2
- Transmission: spread through skin-to-skin contact, usually when skin is broken or lesions present, but asymptomatic viral shedding a possible route of transmission. Neonatal transmission is rare (1 in 10,000 live births), but carries risk of ophthalmic infection ⇒ caesarean section indicated if active blisters at delivery
- Prevention of genital herpes: Condoms with new partner (although doesn't eliminate risk). Avoid sex during an outbreak
- Can have extra genital lesions on thighs and buttocks. Can → radiculoneuropathy → urinary retention/constipation
- Treatment of Genital Herpes (type 1 or 2):
 - Acute: Acyclovir 200 mg 5 times daily for 5 days. Topical creams not effective. Symptomatic treatment: salt bathing, local anaesthetic creams, oral analgesia, oral fluids. Counselling and follow-up important – written information for patients and partners, Herpes Helpline (0508 11 12 13)
 - Suppressive Therapy: Where frequent outbreaks or psychological morbidity. Acyclovir 400 mg BD for up to a year. Can reduce viral shedding by up to 95%
 - Can be devastating. Refer to counselling at Sexual Health Service
- Complications:
 - ↑Risk of AIDS transfer
 - Erythema Multiforme
 - Neonatal Herpes: 1 % transmission but 50% mortality
 - In pregnancy:
 - If first primary episode: miscarriage, prem labour
 - If recurrent, tiny risk for baby
 - If lesions at delivery then Caesarean

Varicella Zoster

- Primary infection: Chicken Pox.
 - Macules → papules → vesicles → crusts
 - Incubation 10 – 21 days (usually 14 – 16)
 - Infectious for 1 – 2 days before rash appears until it crusts over
 - Highly infectious, in hospital requires strict respiratory/contact isolation
 - Complications:
 - Commonly becomes super-infected (eg with scratching) with Staph aureus (or S Pyogenes) which leads to scarring
 - If immunocompromised → overwhelming infection, pneumonitis, hepatitis, encephalitis (treat with Ig and acyclovir)
 - Post-natal infection can be overwhelming
 - Immune response can → encephalopathy with cerebellar ataxia
 - Can lead to severe exacerbation of eczema
 - Then remains dormant in dorsal root ganglia
 - Treatment: Supportive, antipruritic lotion if itchy, cut fingernails short
 - Prevention: Live attenuated virus, or im Ig within 96 hours of exposure if at risk and susceptible (immunocompromised, pregnant, newborn, prem babies)
- Tests: culture – swab transported in viral medium
- Vaccination:
 - Live attenuated vaccine recently licensed for both children and adults
 - Not recommended for general use, but role in protecting non-immune adults (more severe illness)
 - Contra-indicated if immuno-suppressed or pregnant
- **Shingles:**
 - Reactivation of infection: affects 20% at some time. Elderly and immunocompromised are high risk

- Symptoms: Dermatomal pain, then fever malaise for several days, then macule-papules + vesicles, especially in thoracic or ophthalmic division of trigeminal dermatomes. If sacral, then urinary retention may occur. Thoracic (50%), cervical (20%), trigeminal (15%)
- Complications:
 - If shingles around eye (especially end of nose), then are likely to have a dendritic ulcer on cornea. Stain with Fluorescein and shine on blue light, corneal abrasions will shine green. Don't give steroid → blindness. Urgent referral to an ophthalmologist. See Eye Infections, page 144
 - Post-hepatic neuralgia – especially in the elderly and trigeminal
 - Recurrence rare and suggests HIV (or Dermatomal Herpes Simplex)
- Treatment if needed: acyclovir as early as possible, 800mg 5 times a day for 5 days. Pain relief – analgesic or low-dose amitriptyline. Maybe prednisolone to reduce post-herpetic neuralgia. Report visual loss immediately

Epstein Barr Virus

- DNA virus
- One of Herpes Group
- Spread by respiratory secretions (e.g. sneeze, kiss)
- Pre-schoolers an important reservoir: usually just a non-specific URT infection. In later life (e.g. adolescent) get it more acutely plus hepatitis. 1 – 5% present as hepatitis
- Associated with Burkett's lymphoma & nasopharyngeal carcinoma

Clinical

- Highly variable course. Often asymptomatic if < 5 years
- Sore throat (often exudative)
- Fever
- Lymph nodes up
- Tender liver (liver involvement → ↓appetite and ↑feeling unwell), maybe big spleen
- Rash in 10%
- Doesn't resolve (especially after antibiotics)
- Will be tired for weeks/months
- Incubation 30 – 50 days
- Association with symptoms:

	Sore Throat	Lymphadenopathy	Atypical Mononucleosis
EBV	+++	+++	+++
CMV	-	+	+++
HIV	++	++	++
Toxoplasmosis	+	+++	++
Viral Hepatitis	-	+	++

Investigations

- Throat swab
- FBC: may be ↑atypical mononuclear lymphocytes
- EBV serology

Treatment

- Symptomatic
- **Don't** give penicillin if risk of EBV: leads to rash that can be interpreted as penicillin allergy. (E.g. amoxycillin, rash in 80 – 90%)
- Infectious for months. No isolation required
- Steroids if upper airway obstruction in kids

Antibodies to EBV

- IgM Anti-VCA (Virus capsid antigen) and IgG Anti-VCA
 - Usually appear in blood 7 days after symptoms develop in acute primary EBV infection
 - IgM: usually persists for 2 – 4 months
 - IgG: usually persists for life
- Anti EBNA (Epstein-Barr nuclear antigen): Appears 2 months after primary infection and persists for life

- Profiles:

	IgM VCA	IgG VCA	EBNA
No infection	-	-	-
Acute Primary	+	+	-
Past Infection	-	+	+
(ie EBNA +ive rules out acute infection)			

- Paul-Bunell now largely obsolete. Negative in 10 – 15 % of cases

Associated diseases

- Burkett's lymphoma
- Nasopharyngeal carcinoma
- Hodgkin's disease (EBV in 40 – 60% of cases)
- Chronic EBV may occur but is very uncommon (recurrent sore throat, cervical lymphadenopathy)

Chronic Fatigue Syndrome

- Unknown cause: but key differential to EBV

Diagnosis

- Severe chronic fatigue over 6 months or longer, with other known medical conditions excluded, **and**
- 4 of the following during 6 consecutive months:
 - ↓Short term memory or concentration
 - Sore throat
 - Tender lymph nodes
 - Muscle pain
 - Multi joint pain: without swelling or redness
 - Headaches of new type/pattern
 - Unrefreshing sleep
 - Post-exertional malaise lasting > 24 hours

Differential Diagnosis

- Depression
- Psycho-social stressors

Cytomegalovirus (CMV)

- Transmission:
 - Blood: transfusions, intra-uterine, perinatal, needle sharing
 - Cervical secretions and semen
 - Saliva (eg close contact with kids)
 - Urine (eg infants to adults)
 - Organ donation (transplantation)
- Immunocompetent:
 - Kids:
 - Common in preschoolers, usually asymptomatic. May give URTI
 - Prolonged excretion in saliva and urine common
 - Adults:
 - Usually asymptomatic, if not then usually self-limiting
 - May be fever (up to 2 weeks, ie a differential of PUO)
 - Sore throat, cervical lymphadenopathy uncommon
 - Atypical mononucleosis on blood film
 - Differential: EBV, HIV, toxoplasmosis
 - Pregnancy:
 - Congenital infection (ie crosses placenta) in 20 – 40%
 - > 90% show no signs at birth, but watch for long term neurological sequelae (eg sensori-neural deafness, retardation)
 - Severe cases: respiratory distress, jaundice, microcephaly, etc
 - Part of TORCH complex: Toxoplasmosis, Rubella, CMV, HSV
 - Perinatal infection (eg during vaginal delivery):
 - Full term: usually mild

- Pre-term: may be severe
- Immunodeficient:
 - AIDS: one of the most common infections → CMV retinitis (common), CMV encephalitis (rare), CMV colitis (rare)
 - Transplant: greatest risk if they're CMV negative and CMV positive organ → interstitial pneumonia and hepatitis (in liver transplant)
- Transfusion: blood is not routinely screened for CMV antibody. Should give CMV -ive blood to prem babies (<1500 g) and seronegative transplant recipients with seronegative transplants
- Lab diagnosis:
 - Serology:

	IgG	IgM
No infection	-	-
Past infection	+	-
Acute primary or reactivated infection	+	+
- Cell culture – slow (>7 days). Culture lung biopsy or peripheral blood leucocytes
- PCR for CMV DNA on peripheral leucocytes, amniotic fluid, CSF (very specific, less sensitive, very expensive)
- Treatment:
 - Ganciclovir: bone marrow toxicity
 - Foscarnet (nephrotoxic)
 - Ganciclovir prophylaxis used for -ive patients with +ive organs

Parasitology

Toxoplasmosis

- A protozoa/parasite
- Main source: cysts in meat. Also kitten faeces (eg cyst in garden – pregnant gardeners should wear gloves)
- Presentation:
 - Immunocompetent:
 - Lymphadenopathy (eg unilateral)
 - Maybe: fever, myalgia, acute pharyngitis, hepatosplenomegaly, atypical mononucleosis
 - Usually self-limiting – may take months to settle
 - If persistent/recurrent lymphadenopathy → ?Need for treatment
 - Immunodeficient:
 - Acquired or reactivated
 - AIDS most common: CNS involvement (solitary space occupying lesion, encephalitis), also myocarditis, hepatitis
 - Less common in transplants and encephalitis
 - Ocular toxoplasmosis: most cases in adolescents and adults → reactivation infection. → Blurred vision, photophobia, multiple retinal lesions
 - Congenital Toxoplasmosis:
 - 29% fetal infection if mother has primary CMV infection
 - Highest risk in 3rd trimester (1st trimester may miscarry)
 - Complications: spontaneous abortion, premature, still birth
 - Surviving neonates: bilateral choroido-retinitis. In severe cases, TORCH type symptoms
- Lab diagnosis:
 - PCR test for toxoplasmosis: amniotic fluid, CSF (AIDS patients)
 - Lymph node biopsy → characteristic histology
 - Serology:
 - IgM antibody after 5 – 14 days, peaks at 2 – 4 weeks, traces for up to a year
 - IgG: high levels for up to 6 months, declines slowly over years
 - Avidity test: can differentiate between acute phase ‘immature’ IgG and ‘mature’ IgG
- Treatment:
 - Pyrimethamine (Gold standard, but gives bone marrow suppression + give folate) + sulphadiazine (not available in NZ)
 - Pyrimethamine + clindamycin (gives C. difficile diarrhoea)

- Spiramycin (only one safe in pregnancy)

Malaria

- Transmitted by mosquito and very rarely transfusion
- See also Malaria, page 688

Clinical

- Irregular fever – peaks on release of parasite from infected RBCs. May only be mild if person has immunity (ie previous exposure). Various strains have various periodicities
- Chills
- Headache
- Malaise
- Vomiting (20%)
- Diarrhoea (<5%)
- ie similar to Typhoid

History

- Travelled to a malaria country
- What conditions did you stay in, rural/urban, etc
- Was chemoprophylaxis taken, how was compliance
- Diagnosed overseas
- When did you return to NZ (Plasmodium Falciparum usually in 1 month, P Vivax up to a year)
- Length of illness

Diagnosis

- Blood film for plasmodium protozoa: a thick film is necessary as well as the standard thin film if parasites are scant (eg if have some immunity)
- Pointless if patient is afebrile
- If initially negative, repeat 12 hourly for 48 hours
- Critical that you find out which plasmodium species is present, eg:
 - Plasmodium Falciparum: common in Africa, can cause cerebral malaria (fatal)
 - Plasmodium Vivax: more common in Asia/Oceania
- Features of poor prognosis:
 - CNS signs: disturbed consciousness, repeated convulsions
 - Respiratory distress
 - Haemorrhage, shock
 - Biochemical markers: ↑Cr, ↓HCO₃, ↑bilirubin, ↓glucose
 - High parasitic load

Prevention

- Assessment of risk:
 - Malaria geography: transmission rates vary by country (eg high in Sub-Saharan, PNG, Solomon Islands)
 - Likely extent of contact with mosquitoes (eg standard of accommodation)
- Anti-mosquito measures: long sleeves & trousers, insect repellent/sprays, nets
- Chemoprophylaxis:
 - Start 1 week beforehand and continue till 4 weeks after leaving
 - Mefloquine (effective against chloroquine resistant P Falciparum).
 - 250 mg *weekly*
 - Side effects: nausea, diarrhoea, dizziness – usually self-limiting.
 - At higher doses (eg for treatment) convulsions and sinus bradycardia
 - Contraindications: drugs altering cardiac conduction, psychiatric disease, epilepsy, pregnant, kids < 5kg, or where fine CNS co-ordination required (eg airline pilots)
 - Doxycycline, 100 mg *daily*
 - After food otherwise gastritis
 - In rural areas of SE Asia, where mefloquine-resistant strains of P falciparum are reported
 - Contraindicated in pregnancy women and children
 - Chloroquine + proguanil: Only one safe for first trimester. Low efficacy against drug resistant falciparum

- Chloroquine weekly – countries without chloroquine-resistant *P falciparum* (Central America north of Panama)

Treatment

- P Vivax, P Ovale, P Malariae:
 - Acute treatment: 3 days of Chloroquine
 - For radical cure in P Vivax or P Ovale:
 - Primaquine for 2 weeks (screen for G6PD deficiency first)
 - Eradicates exo-erythrocytic liver cycle. If you don't, they will relapse
 - Relapse common (20%) – maybe several months later. If so, repeat 3 days of Chloroquine followed by 2 weeks of higher dose of Primaquine
- P Falciparum:
 - Quinine sulphate + Doxycycline for 7 days
 - No persisting cycle so relapse not a problem
 - Cerebral malaria: iv quinine: loading dose then maintenance infusion
- Drug resistance:
 - Chloroquine-resistant strains of plasmodium falciparum are widespread
 - Chloroquine-resistant strains of P Vivax reported in Indonesia and PNG

Other

Amoebiasis (Entamoeba histolytica)

- Diagnosis:
 - Intestinal amoebiasis: stool sample * 3, 48 hours apart, in PVA fixative
 - Cysts: frequently present asymptotically (carrier state)
 - Extra-intestinal amoebiasis (eg amoebic abscess of the liver) maybe months later. Serum antibody test
- Treatment:
 - Intestinal amoebiasis: metronidazole then diloxanide furoate
 - Extra-intestinal: metronidazole (surgical drainage may be necessary)
 - Asymptomatic: Diloxanide furoate

Giardiasis

- Diagnosis:
 - Stool examination for Giardia Lamblia cysts, 3 samples 48 hours apart
 - Duodenal aspirate and direct examination for trophozoites
- Treatment:
 - Tinidazole 2g stat or Metronidazole 400 mg 8 hourly for 7 days
 - Test for cure with repeat stool sample. Relapse not uncommon

Filariasis

- Commonest is Wuchereria bancrofti imported from Samoa
- → Elephantitis
- Diagnosis: Blood sample
- Treatment:
 - Ivermectin
 - Most cases are asymptomatic or low grade pyrexia and don't require treatment
 - If severe, surgical relief of major lymphatic obstruction may be necessary

Intestinal Worms

- Hookworm:
 - Ancylostoma duodenale, necator americanus
 - Diagnosis: stool sample * 3
- Roundworm:
 - Ascaris Lumbricoides
 - Diagnosis: worms passed in faeces, or stool samples * 3 and examine for Ova
- Pinworm:
 - Enterobius vermicularis
 - Diagnosis: sellotape swabs of anus

- Whipworm:
 - *Trichuris trichura*
 - Diagnosis: stools * 3
- Treatment: mebendazole 100mg BD for 3 days for Hookworm, Roundworm, Pinworm (treat whole family) and whipworm (only if severe)
- Strongyloides Stercoralis:
 - Diagnosis: Stools * 3
 - Treatment: Thiabendazole
- Tapeworms:
 - *Taenia saginata*, beef tapeworm
 - Diagnosis: Stools * 3, examine for worm segments
 - Treatment: niclosamide

Hydatid Disease

- Aetiology: *Echinococcus granulosus* (a flatworm). Infected from ova excreted in dog faeces. Dogs infected from eating raw sheep offal (ie liver) containing hydatid cysts
- Clinical: Often acquired in childhood, present in older age with solitary cysts (liver, lung, brain)
- Treatment: surgical drainage + albendazole as adjunct
- Diagnosis: Serology: haemagglutination test + complement fixation test

Cryptosporidium

- Common protozoan parasite
- Profuse watery diarrhoea for 48 hours. Very common cause of diarrhoea.
- Severe and persisting cases in AIDS
- Diagnosis: Stool microscopy with ZN stain for acid fast cysts
- Treatment: Paromomycin (an oral, non-absorbable aminoglycoside) has some efficacy

Pneumocystis Carinii

- Protozoan parasite probably part of normal respiratory flora
- Causes interstitial pneumonitis in immuno-compromised patients (transplant, leukaemia, AIDS)
- Diagnosis: Bronchial lavage or open lung biopsy
- Treatment: Cotrimoxazole (alternatively pentamidine). Relapse in 25%
- See also Other pneumonias, page 70

Travel Medicine

- Travel History:
 - Where are you going
 - How are you getting there
 - How long there
 - What will you be doing
 - Where are you staying
 - Have you been there before
- Examples:
 - 3 week package to Hong Kong, Singapore, Bangkok: Hep A and Tetanus up to date. Typhoid is overkill
 - 4 month Overland through from Thailand to Turkey (Vivax Malaria): Malaria, Hep A, Tetanus
 - 3 month TI in Tanzania: Hep A, Typhoid, Yellow fever (not Asia)
 - 3 year diplomatic posting in PNG: Malaria prophylaxis if going rural but not continuously

Vaccination

- Malaria chemoprophylaxis: unnecessary if in a malarious country for < 7 days. Risk in main resort areas of Asia is low
- Typhoid:
 - Injectable: salmonella typhi antigen, 70% protection for 3 years
 - Oral vaccine: attenuated live strain, doses at 0, 3 and 5 days gives protection for one year. Useful at short notice
- Yellow Fever:
 - Attenuated live strain (\Rightarrow not if immunocompromised)

- For travel to equatorial Africa and South America
- Protection for 10 years
- Requires special certificate, stamp, etc ⇒ only done in designated centres
- Polio:
 - OPV: Oral: 2 drops po (tiny risk of giving it to adults if no previous vaccine ⇒ use IPV)
 - IPV: Inactivated polio vaccine: 0.5 mls sc
 - Booster every 10 years
- Tetanus/Diphtheria Toxoid: booster every 10 years. 0.5 mls im into deltoid muscle
- Meningococcal Vaccine: For types A, C, W, Y – not B. sc injection gives 3 years protection. Indicated for travel to countries where epidemics occur – Nepal, West Africa, Brazil
- Hepatitis A: Formalin inactivated HAV. IM injection gives protection for one year. Booster dose 6 – 12 months later gives long-term protection. If over 50, check immune status – may be immune and therefore won't need it (its expensive)
- Japanese Encephalitis Vaccine: Widespread through SE Asia. Rare for travellers to get it – but high mortality. Side effects from vaccine
- Rabies: Only for people intending to work longer term in rural/agricultural areas of Asia

Pyrexia of unknown origin if returning from 3rd world

- Diagnose on blood film/culture:
 - Malaria
 - Dengue
 - Typhoid: usually constipated, used to die of peritonitis, bradycardia, high spiking fever, takes days for temperature to go down
- Ross River
- Syphilis
- Filariasis (eg Samoa)
- Other imported infections from Pacific:
 - Leprosy (mycobacterium leprae)
 - Yaws (Treponema pertenue)
 - Eosinophilic Meningitis

Antibiotic Treatment

Summary

G +ive		
Cocci	Strep pneumonia	Oral: Amoxycillin. IV: Penicillin G Allergy: Erythromycin. Resistant (eg kids): Ceftriaxone Resistant and Meningitis: Cefotaxime + Vancomycin (act synergistically) Resistant and Endocarditis: Vancomycin
	Strep faecalis	Trimethoprim
	Strep agalactiae	Penicillin. [β haemolytic. Normal vaginal flora]
	Strep pyogenes	Penicillin. Erythromycin if allergic. Also sensitive to flucloxacillin
	Strep sanguis	Penicillin [α haemolytic]
	Staph aureus	Flucloxacillin. Allergy: Ceftriaxone. MRSA (resistant to penicillins and cephalosporins): Vancomycin
	Staph epidermidis	Flucloxacillin. Resistant: Vancomycin
Bacilli	Listeria monocytogenes	Amoxycillin. Elderly/immunocompromised: ciprofloxacin (quinolone – not in kids)
	Clostridium difficile	Metronidazole
	Enterococcus faecalis	Amoxycillin
G -ive		
Bacilli	E Coli	Trimethoprim. Cotrimoxazole (trimethoprim + sulphmethoxazole), Norfloxacin (Quinolone). 48% resistant to amoxycillin. Augmentin resistance growing. Meningitis: Cefotaxime (good CSF penetration). Consider gentamycin or cotrimoxazole
	Campylobacter Jejuni	Erythromycin

	H Influenzae	Cefaclor, Augmentin, Tetracycline 5% resistant to penicillin, not sensitive to erythromycin
	Legionella	Erythromycin. Add rifampicin if severe
	Pseudomonas Aeruginosa	Ciprofloxacin. Maybe Tobramycin or piperacillin
	Gardnerella Vaginalis	Meningitis: Ceftazidime Metronidazole. Metronidazole is otherwise inactive against aerobes
	Bordetella Pertussis	Erythromycin
	Branhamella Catarrhalis	Augmentin, cefaclor, tetracycline, cefuroxime 70% penicillinase
Anaerobes	Bacteroides Fragilis	Metronidazole. Not penicillin or cephalosporins
	Helicobacter Pylori	Clarithromycin + metronidazole + omeprazole (7 days)
Cocci	Neisseria Meningitidis	Penicillin. Cefotaxime if allergic. Prophylaxis: Rifampicin, ceftriaxone if pregnant
	Neisseria Gonorrhoea	Stat: Amoxycillin + Probenecid Ciprofloxacin or tetracycline if penicillin allergy or resistant. Azithromycin if concurrent chlamydia or pregnant
Not G-ive	Chlamydia Pneumoniae	Erythromycin
	Chlamydia Trachomatis	STD: Doxycycline, azithromycin, pregnancy: Erythromycin PID: Erythromycin + ornidazole NB: Obligate intracellular parasite. Cellular wall similar to G-ive but not actually a G-ive bacteria
Others		
	Mycoplasma	Erythromycin. 2 nd line: Tetracyclines (eg doxycycline) except pregnant/kids
	TB	Rifampicin + isoniazid + pyrazinamide (also ethambutol if isoniazid resistant). Prophylaxis: rifampicin
	MAC	Clarithromycin
	Treponema pallidum	= Syphilis. Penicillin G. Resistant: Tetracyclines (eg doxycycline)
Yeasts		
	Aspergillus	Amphotericin B. Itraconazole prophylaxis
	Cryptococcus neoformans	Fluconazole (good CSF penetration), Amphotericin B
Virus		
	HSV	Acyclovir
	CMV	Ganciclovir
	Toxoplasmosis	Pyrimethamine + clindamycin. Pregnant: Spiramycin
Protozoa		
	Cryptosporidium	Nothing effective. Maybe Paromomycin (oral, non-absorbed aminoglycoside)
	Giardiasis	Tinidazole stat or metronidazole 7 days
	Trichomonas	Doxycycline, Metronidazole
	Pneumocystis Carinii	Cotrimoxazole
	Pneumonia	
	Malaria Prophylaxis	Mefloquine weekly: good for chloroquine resistant falciparum. Not epilepsy, pregnant, babies Doxycycline daily: Esp Mefloquine resistant falciparum. Not kids or pregnant Chloroquine + Proguanil: if pregnant Chloroquine weekly: if no chloroquine resistant falciparum
	Plasmodium Falciparum	Quinine sulphate + doxycycline
	Plasmodium Vivax	Chloroquine 3 days then primaquine 2 weeks
	Amoebiasis	Metronidazole + diloxanide furoate
Worms		
	Filariasis	Ivermectin
	Intestinal worms	Hookworm, roundworm, pinworm: Mebendazole Strongyloides Stercoralis: Thiabendazole Tapeworms: Niclosamide

Antibacterials

Penicillins

	Use for	Notes
Penicillin G (iv/im) (Oral form: Pen V)	Streptococci Staphylococci N Gonorrhoeae N Meningitidis T Pallidum Leptospira Syphilis Anaerobes	Not Enterococcus faecalis, resistance in kids to strep pneumoniae But 80% produce penicillinase Some produce penicillinase
		Peptostreptococci, Clostridia, Fusobacteria, Bacteroides (not B fragilis), Actinomyces
Amoxycillin	As above plus: Enterococcus faecalis Listeria monocytogenes Haemophilus influenzae Some E coli Most Proteus mirabilis	6 % produce penicillinase 48% resistant 20% produce penicillinase
Augmentin		Clavulanic acid inhibits penicillinase. Principle use is infectious exacerbations of chronic bronchitis
	Haemophilus influenzae Branhamella Catarrhalis	Increasing E coli resistance
Flucloxacillin	Staph Aureus	Penicillinase producers. MRSA resistant to Flucloxacillin and cephalosporins
Piperacillin Tazocin	Pseudomonas aeruginosa Neutropenic cancer patients	Systemic infection only = Piperacillin + Tazobactam (a beta-lactamase inhibitor)

Cephalosporins

Gen	Examples	Use for
1	Cefazolin Cephalothin (IV) Cephadrine (IV & oral) Cephalexin (oral)	<ul style="list-style-type: none"> Better for G+, poor for G- Gram +ives: Streptococci (not E faecalis), Staphylococci, Anaerobes (Not B Fragilis) Gram -ives: Some coliforms: E coli (20% resistant), Klebsiella Inactive against: H Influenzae, Pseudomonas, Enterococcus faecalis
2	Cefuroxime (IV+oral) Cefamandole (IV+IM) Cefaclor (Oral)	<ul style="list-style-type: none"> G +ive: as for 1st generation G -ive: Better against coliforms Active against H influenzae Inactive against: Pseudomonas, E Faecalis, B Fragilis
3	Ceftriaxone Cefotaxime Ceftazidime Cefpodoxime (oral)	<ul style="list-style-type: none"> Good activity against most coliforms Activity against G+ < 2nd generation No activity against Bacteroides or Enterococcus Ceftazidime good against pseudomonas aeruginosa Ceftriaxone has long T½, can be given once daily Good CSF penetration ⇒ first choice for meningitis caused by coliforms or HIB
4	Cefipime Cefpirome	<ul style="list-style-type: none"> Highly stable against β-lactamases Good against most aerobic G -ives (coliforms and <i>pseudomonas</i>) Good against G +ive, incl staph aureus (similar to 1st generation) but not Enterococcus
	Cefotetan	<ul style="list-style-type: none"> Broad spectrum cephemycin Good against Bacteroides and Coliforms (not pseudomonas) Indications: antibiotic prophylaxis for colonic and gynaecological surgery

Aztreonam	<ul style="list-style-type: none"> Active against G-ive bacteria only: including coliforms and to a lesser extent Pseudomonas Indication: less toxic than aminoglycosides for G-ive infection
Imipenem Meropenem	<ul style="list-style-type: none"> A carbapenem (not cephalosporins) Inhibit nearly all G+ and G- Restricted as its so good Indication: Empiric therapy in neutropenic cancer patients

Macrolides

- Effective against:
 - Staph aureus (up to 10% resistance in community strains)
 - Streptococci (not E faecalis)
 - Anaerobes (only moderately effective against B fragilis)
 - Mycoplasma pneumoniae
 - Chlamydia pneumoniae
 - Chlamydia trachomatis (but tetracycline is the drug of choice)
 - Campylobacter jejuni
- Ineffective against:
 - H influenzae
 - No CSF penetration
- Indications:
 - Treatment of susceptible bacteria if penicillin allergy
 - Atypical pneumonia (eg Mycoplasma, Chlamydia or Legionella)
 - Campylobacter
 - Chlamydia infection in pregnant women
- Erythromycin**
- New analogues:
 - Roxithromycin (Rulide)
 - Clarithromycin** (Klaricid): Treatment of MAC, especially in AIDS patients
 - Azithromycin (Zithromax): Single dose treatment for STD's caused by Chlamydia trachomatis or N. gonorrhoeae (especially in pregnancy)

Vancomycin

- G+ive wonder drug – active against G+ive only
- Indications:
 - Systemic infections caused by MRSA or MRSE (Epidermidis), or infected Hickman lines in cancer patients
 - Infective Endocarditis due to Strep or Staph with penicillin allergy
 - Clostridium difficile colitis (by mouth). First line is metronidazole
- Ototoxic and nephrotoxic
- Teicolpanin: similar drug, active against some Vancomycin Resistant Enterococci (VRE)

Rifampicin

- Always used in combination (except meningitis prophylaxis)
- Active against M. Tb, Staph aureus, Legionella
- Indications:
 - TB (in combination)
 - Severe Staph aureus infections (eg infective endocarditis) in combination
 - Severe legionella pneumonia (in combination with erythromycin)
 - Prophylaxis against N meningitidis or HIB

Aminoglycosides

- Active against all coliform bacilli (eg E Coli), pseudomonas, staphylococci
- Inactive against: streptococci, anaerobes
- Indications: G- sepsis, perforated appendix
- Drugs:
 - Gentamicin**
 - Tobramycin**: more active against pseudomonas
 - Amikacin: reserved for Gentamycin resistant bugs

- Spectinomycin: N gonorrhoeae (penicillinase producers)
- Otto and nephrotoxic

Cotrimoxazole

- = Trimethoprim + Sulphamethoxazole
- Broad spectrum: Staph, Strep, many coliforms (not Pseudomonas), HIB, Pneumocystis, Brucella
- Indications: Acute infectious exacerbations of chronic bronchitis, PCP in AIDS
- **Trimethoprim** on its own is the standard treatment against community acquired UTI (E Coli, Klebsiella, Proteus, Strep faecalis)

Quinolones

- Broad spectrum oral antibiotic
- Active against: most coliforms, pseudomonas aeruginosa (main use), Staphs (including MRSE and MRSA), N gonorrhoeae, HIB, Branhamella catarrhalis (good), Salmonella, Shigella, Yersinia, Campylobacter
- Poor activity against Anaerobes, streptococci
- Can damage growth cartilage ⇒ not licensed for children
- Indications:
 - **Norfloxacin:** resistant UTIs
 - **Ciprofloxacin:** Mainly pseudomonas

Tetracyclines

- Eg **doxycycline** (once a day on full stomach), very common in treatment of STIs
- Active against Staphs, Streps, Coliforms, HIB
- Other indications:
 - Syphilis and Gonorrhoea if penicillin allergy
 - Mycoplasma pneumoniae
- Contraindications: young children, pregnancy, renal failure (except doxycycline)

Metronidazole

- = Flagyl
- Active against all anaerobes (eg B fragilis)
- Inactive against aerobes (excl Gardnerella vaginalis, causing bacterial vaginosis, where it is drug of choice)
- Active against Protozoa: Trichomonas vaginalis, Giardia lamblia

Other

- Fucidin: active against Staph Aureus, must be used in conjunction with, eg Flucloxacillin. Use in bone/joint infections
- Chloramphenicol: for infections caused by Burkholderia cepacia

Antifungals

- **Nystatin** (topical): vaginal or oral candida
- **Miconazole** (topical): Candida and dermatophytes (except scalp or nails)
- **Terbinafine** (oral) Dermatophyte infections of scalp or nails (has superseded Griseofulvin)
- **Itraconazole** (oral): Dermatophyte infections of scalp or nails, prophylaxis in Candida and Aspergillus in immunocompromised
- **Fluconazole** (Oral/IV): active against yeasts (candida, cryptococcus). Good CSF penetration (eg Cryptococcal meningitis)
- **Amphotericin B** (IV): Very good but side effects, including nephrotoxicity
- See also Antifungals, page 336

Antivirals

- **Acylovir**: active against HSV and VZV (less active)
- **Ganciclovir**: CMV in immunocompromised patients. Bone marrow suppression → neutropenia

Vaccination

- Reference: Public Health Module Notes

Vaccination Principles

- Jenner first vaccinated using cowpox against smallpox in 1796
- Characteristics of immunity:
 - Specificity: response to specific antigen
 - Priming
 - Memory: brisk secondary response
- Results of vaccine:
 - Most stimulate serum antibodies (IgG, IgM)
 - Some stimulate IgA (eg polio, rubella)
 - A few promote cell mediated reaction (eg BCG)
- Types of vaccine:
 - Live attenuated vaccine (eg OPV, MMR, VZ, BCG): full and long lasting immunity after a single dose (except OPV which requires 3 doses)
 - Inactivated vaccines:
 - First dose gives a predominantly IgM response. Further doses raise IgG level (depending on potency of the vaccine, maturity of the immune system and time interval)
 - Inactivated whole bacteria or viral vaccines: IPV, Hep A, Whole cell pertussis (being replaced).
 - Modified toxins (toxoids) eg Diphtheria, Tetanus → antibody response to toxin not infective agent
 - Sub-unit vaccines: eg Hep B, HIB, Pneumococcus, Influenza – the main focus of modern vaccines – conjugated vaccines with fewer side effects and easy to grow from genetically engineered yeasts etc.
 - Also passive immunity available from injectable IgG. Immediate protection lasting from weeks to months
- Population protection:
 - Immunisation is delivered to individuals and provides individual protection and benefit
 - Also provides population protection (herd immunity):
 - Some level of immunisation protects unimmunised people who would otherwise have caught it ⇒ don't need to immunise those for whom its contraindicated (eg too young or sick)
 - ↑Virulence ⇒ ↑coverage necessary to get herd immunity
 - 'Free riders' – because they perceive costs (needles, hassle, side effects) to be greater than perceived benefits → weakens herd immunity
- Efficacy and effectiveness:
 - Efficacy: Does intervention provide a specific outcome (eg an IgG response) under ideal lab circumstances
 - Effectiveness: Does it work under normal clinical circumstances
 - Apparent paradox: as coverage ↑, so does the proportion of cases that have been vaccinated (but lower absolute numbers of disease), due to vaccination failure. Can create the illusion that the vaccine is ineffective
- Vaccine failure:
 - Primary vaccine failure: inadequate physiological response to the vaccine (eg freezing or overheating of the vaccine, or poor host response)
 - Secondary vaccine failure: waning immunity
- Degrees of protection:
 - Generally provides 80 – 95% protection (BCG 50%, Influenza 70%)
 - May protect against severe disease rather than infection (eg Diphtheria)
- Vaccination coverage:
 - = Proportion of a population who have completed a specific course of immunisation
 - In Northern Region in 1996, 63% by 2 years but only 45% for Maori and 53% for Pacific islanders
 - With measles: ↑coverage → ↑time between epidemics as need a pool of 130 – 150,000 measles susceptible children to sustain an epidemic. Each epidemic → 50,000 kids contract measles and therefore immune in future. 10,000 unprotected kids added to the pool each year.
 - Policy measures: revise schedule to reduce the number of visits, immunisation certificates on enrolment at school/early childhood centre.
- Surveillance: Generally poor systems
 - Disease surveillance: notifications, discharge and mortality database, outbreak investigations, disease modelling

- Coverage surveillance: registers and periodic surveys
- Adverse event surveillance
- Cold-chain monitoring

Vaccination Practice

- Practical vaccination standards:
 - Ensure correct storage and transport: maintain the ‘cold chain’ at 2 – 8 C. Eg have dedicated fridge and check its minimum and maximum temperature daily
 - Check vaccines due for each patient: either age groups (neonates, children, adolescents, adults, elderly) or specific exposure situations (occupational, travel, post-exposure)
 - Discuss and obtain informed consent: Written consent only required for children if care giver not present
 - Check contra-indications
 - Administer vaccine
 - Manage adverse reactions:
 - Observe for 20 minutes afterwards
 - Local or systemic reactions (fever, rash, joint pains): symptoms of immune activation. Offer Paracetamol. Especially whole cell pertussis. MMR may be followed about 7 – 10 days later by a 2 – 3 day fever and rash (but the vaccine is not infectious)
 - Anaphylaxis: Distinguish from fainting (which is common). Treatment: ABC, Adrenaline 1:1000 IM injection, 0.01 ml/kg, O₂
 - Report to centre for Adverse Reaction Monitoring if serious (includes persistent screaming > 3 hours and > 5 cm swelling at injection site), but also convulsions, meningitis within 30 days
 - Manage records: practice notes, HBL claim record and immunisation certificate for parents
- Anti-immunisation views:
 - Risks outweigh benefits: some diseases now rare and specific vaccines have serious side effects
 - Alternative health views: disease part of growing up (so was death!) and natural infection develops immune system
 - Plus a variety of beliefs/values that will be hard to shift
 - Main reasons for non-immunisation is ‘passive rejecters’ – don’t get around to it
- Contraindications:
 - Acute illness or fever > 38 C: defer vaccine. Otherwise will blame the illness on the vaccine!
 - Living with an immune suppressed person: use IPV rather than OPV
 - Reaction to previous dose: encephalopathy with 7 days of DTP vaccines or immediate severe allergic reaction. If true anaphylaxis seek specialist advice
 - Immune suppression: don’t give live vaccine. Likely to have reduced response to inactivated vaccines
 - Pregnancy: theoretical risk from live virus vaccines
 - If in doubt, refer to a paediatrician
- False contraindications:
 - Mild illness, URTI, fever < 38.5 C
 - Asthma, hay fever, eczema
 - Prematurity and low birth weight in an otherwise healthy child – these especially need vaccination
 - Previous clinical history of illness: no harm done from vaccinating and many clinically diagnosed cases of an illness are in fact something else
 - On antibiotics, inhaled or low dose steroids
 - Stable neurological conditions (cerebral palsy, Down)

Currently Vaccine Schedule

- Current Vaccination Schedule from February 2002:
 - Covers Hep B, Diphtheria (child dose = D, adult dose = d – smaller), Tetanus, acellular Pertussis, Polio (now all intravenous = IPV, not oral), Hib, Measles, Mumps, Rubella

	DTaP- IPV	Hib- Hep B	Hep B only	IPV	MMR	DTaP- Hib	Td	Influenza
6 weeks	✓	✓						
3 months	✓	✓						
5 months	✓		✓					
15 months					✓	✓		
4 years	✓					✓		
5 years								
11 years				If not had 4 doses			✓	
45 years							✓	
65 years							✓	✓

- For unimmunised adults:
 - Give jabs over same timeframe
 - Don't need HIB, don't give paediatric dose of diphtheria (too big) and more inclined to use IPV
- Additional vaccination in specific age groups:
 - Neonates:
 - Babies of HBsAg +ive mothers: Hepatitis B immune globulin (HBIG) and vaccine at birth, vaccine at 6 weeks, 3 months and 5 months. Also offer vaccination to household and sexual contacts.
 - BCG if possible Tb exposure
 - Women of child bearing age who are susceptible to Rubella should be offered MMR
 - Adults: Td (after injury and at 45 and 65 – used to be 10 yearly) + annual influenza
 - Elderly: annual influenza + pneumococcal (5 yearly)
- Specific exposure situations:
 - Splenectomy: Pneumococcal vaccine
 - Occupational: Health care workers (eg Hep B) or HAV to food workers
 - Travel: See Travel Medicine, page 510
- Future Developments:
 - Inclusion of Varicella Zoster and pneumococcal for children
 - Research into Group B meningococcal (currently 10 year epidemic, 250 cases per year), Rotavirus and RSV, non-infectious diseases including cancer

Vaccine Preventable Diseases

- Measles and Pertussis are the main ones still happening that we shouldn't have
- **Hepatitis B:** See Hepatitis B, page 187
- **Diphtheria:**
 - Corynebacterium diphtheriae → respiratory and cutaneous infection (grey membrane on throat). Exotoxin causes cardiac toxicity and ascending paralysis. Spread by nasal droplets
 - 1 imported case in last 20 years. Till 1945 killed 100 babies a year. High in USSR in 90s.
 - Vaccine: inactivated diphtheria toxoid, boosters every 10 years. > 80% efficacy
- **Tetanus:**
 - Clostridium tetani from soil and animal faeces → muscular rigidity due to neurone specific toxin, 10% mortality
 - 3 notifications per year (old ladies in the garden). Common in environment ⇒ no herd immunity
 - Vaccine: Inactivated toxoid, boosters every 10 years, 100% efficacy
- **Pertussis:** See Pertussis, page 609
- **Polio:**
 - Enterovirus spread by faeces and saliva
 - Presentation:
 - Usually asymptomatic or mild (fever, headache, nausea, vomiting)
 - Only 1% of infected get severe clinical disease: severe muscle pain, neck and back stiffness → flaccid paralysis
 - Last wild virus infection in 1962. Occasional imported and vaccine associated cases
 - Vaccine:

- Live oral polio (OPV) > 90% protection after 3 doses. < 1% of recipients develop diarrhoea, headache or muscle pains. 1 in 2.5 million recipients or close contacts develop paralysis (more common in immunosuppressed) = Vaccine Associated Polio Paralysis (VAPP)
- Inactivated polio vaccine (IPV) for immunocompromised (will be used more widely when it can be combined with other jabs)
- **Haemophilus influenzae type B** (HIB): See Epiglottitis, page 609
- **Measles:** See Measles, page 617
- **Mumps:** See Mumps, page 617
- **Rubella:**
 - Togavirus spread by nasal droplets
 - Presentation:
 - Incubation 2 – 3 weeks
 - Fever, headache, mild conjunctivitis, erythematous maculo-papular rash, lymphadenopathy (especially posterior triangle), arthritis, arthralgia
 - 50% develop the rash and lymphadenopathy
 - 50% of adolescents and adults have arthralgia or even frank arthritis
 - 1 in 5,000 have encephalitis
 - Complications:
 - Congenital rubella syndrome: 90% of embryos of mothers infected in 1st trimester will abort or have major abnormalities (severely retarded, seizures, deafness, cardiac defects). Frequent problems after birth
 - Rate of congenital rubella is 5 times the US rate
 - ~ 60 notifications per annum (1600 in 1995)
 - Vaccine:
 - 98 % protective
 - To protect the unborn child only – relies on herd immunity. Need to vaccinate guys as well otherwise they will maintain a population reservoir which women with vaccine failure will catch
 - 5% of adolescents and adults have arthralgia and 1% have non-infectious rash
 - Contra-indicated in pregnancy and immunosuppressed
- **Influenza:**
 - Virus types A (H3N2 and H1N1) and B
 - Causes Fever, rigors, headache, myalgia, prostration. Estimated 400 deaths per annum.
 - Vaccine: inactivated subunit vaccine for new strains (resulting from ‘antigenic drift’). 60 –90% effective. Contraindicated if egg allergy
 - Pandemics result from ‘antigenic shift’
- Tb: **BCG:** See Mycobacteria, page 502
- **Pneumococcal Disease:** See Streptococcus Pneumoniae, page 501
- **Varicella Zoster:** See Infectious Diseases, page 504

Pharmacology

- Generally, specific drugs are covered in the relevant systems chapter
- Specific topics elsewhere:
 - Antibiotics in infectious diseases, see Antibiotic Treatment, page 511
 - Anticoagulant Treatment, page 75
 - Antidepressant and Mood Stabilising Medication, page 432

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Pharmacokinetics

- Deals with time course of the drug in the body:
 - Absorption: rate and amount absorbed
 - Distribution: amount in the body/volume of distribution
 - Elimination = Clearance: rate of metabolic and renal elimination
- Drug concentration usually plotted as plasma concentration versus time

Variability of Drug Response

- Disease, patient and doctor specific factors leading to the prescribing decision
- Absorption: formulation, GI motility, polypharmacy (eg Grapefruit juice)
- Distribution (ie Vd)
- Plasma protein binding (generally not important unless highly bound and low Vd)
- Metabolism: age, genetic factors, enzyme induction and inhibition, first pass metabolism, dose-dependent metabolism, active or toxic drug metabolites, biliary excretion, renal elimination
- Tissue Sensitivity

Volume of Distribution (Vd)

- Volume of distribution = volume into which the drug appears to be uniformly distributed with a concentration equal to that of plasma
- Relates the amount of drug in the total body relative to that in the plasma. Explains where drug goes – not what it does. In one compartment model:
 - $V_d = \text{dose/plasma concentration L/kg}$, or
 - Amount in body = $V_d * \text{conc}$
 - $V_d = Cl/Ke$
- Examples:
 - Gentamycin has an apparent Vd of extracellular H₂O
 - Digoxin has a Vd much larger than physical volume of body
 - Warfarin has a much smaller Vd than expected
- Use Vd to calculate loading dose: **LD = Vd * target conc**
- Vd can be altered in cardiac, liver and renal disease and in obesity
- For obese patients, use total body weight for lipid soluble drugs and ideal weight for water-soluble

Clearance (Cl)

- = Elimination
- Clearance of drug corresponds to the volume of plasma that appears to be cleared of its drug in unit time e.g. mls/min, l/hr.
- Represents the size of the plug hole, rate of elimination (= rate of clearance) is the flow through the plug hole
- Depends on rate at which drug is transported to the organ of elimination and the efficiency of the eliminating organ in removing the drug
- Clearance = rate of elimination/drug concentration (as long as not saturable elimination, eg phenytoin, alcohol)
- Clearance can be:
 - Concentration dependent/ Capacity limited: saturable metabolic pathway (eg phenytoin)
 - Flow-dependent: organ elimination rate = concentration * flow * extraction ratio (fraction cleared on each pass through the organ). Eg will be eliminated on 1st pass \Rightarrow elimination dependent on blood flow. If Heart failure \rightarrow ↑ vasoconstriction to maintain blood flow \rightarrow ↓ liver flow \rightarrow ↓ elimination (eg lignocaine, propranolol). Total body clearance can't exceed cardiac output (5 l/min)
- Clearance and Volume of Distribution are independent of each other, but T½ is dependent on both
- **Maintenance Dose = clearance * desired concentration**
- Compartments:
 - One or multi compartment models
 - K_a = absorption into compartment
 - K_e = elimination from compartment

Linear kinetics

- First order kinetics: rate of transport or elimination proportional to drug concentration in the compartment
- Zero order kinetics: elimination has maximum value → rate is non-linear and it's a capacity limited process. Eg alcohol is metabolised at 10 ml/hr. Beyond this the enzyme metabolism is swamped. So if dose rate is greater than clearance rate, then a small increase in dose rate leads to a dramatic increase in plasma concentration (ie accumulation)

Michaelis-Menten kinetics

- For a drug that undergoes zero-order elimination, when the concentration is low enough, elimination no longer occurs at its maximum rate (V_{max}) but at a rate dependent on but not proportional to the plasma concentration. As the concentration reaches $\frac{1}{2}$ the maximum rate (k_m), first order elimination occurs
- So, elimination will increase with increasing dose, but not proportional to the dose
- Zero-order kinetics will be approached → risk of accumulation
- Issue for any drug having zero-order kinetics within its therapeutic range
- E.g. salicylic acid (especially in overdose), phenytoin, alcohol

Half Life ($T_{1/2}$)

- Time for drug concentration to decline by half \Rightarrow influences dosing interval
- Is dependent on clearance and volume of distribution:
$$V_d = T_{1/2} * \text{clearance} / 0.693$$
- Rate at which drug leaves the body is dependent on C_l & V_d . In one compartment model:
$$K_e = C_l/V_d$$
- = Measure of how the whole body handles the drug – how quickly it gets out
- But it doesn't work in practice...
 - For slowly excreted drugs, $5 * T_{1/2}$ and it will be eliminated for practical purposes
 - But for anaesthetic drugs that you want to switch on and off quickly the therapeutic window is often in the redistribution phase – not the elimination phase. Need a more complex model where the drug redistributes to (then from) slow and fast compartments, as well as being excreted from blood \rightarrow context sensitive half-life. If drug is over infused, it builds up in other compartments and then takes a long time to wash out. So give a reducing amount over the duration of infusion as other compartments get saturated and stop 'sucking it out' of blood

Steady State Concentration

- Amount of drug absorbed = amount eliminated
- Takes 5 half lives to reach 97% of steady state, if each new dose given at half life spacings
- The shorter the $T_{1/2}$, the sooner the C_{ss} will be reached (steady state concentration)
- The shorter the $T_{1/2}$, the greater the plasma concentration will fluctuate between doses
- If $T_{1/2}$ is prolonged, dose should be reduced or dosage interval increased
- $C_{ss} = (F * D) / (C_l * T)$ where F = bioavailability, D = dose, C_l = clearance and T = dosage interval

As $C_l = (V_d * 0.693) / T_{1/2}$, then

$$C_{ss} = (F * D * T_{1/2}) / (0.693 * V_d * T)$$

Bioavailability (F)

- = Fraction of drug that reaches the systemic circulation
- $F = AUC$ (Area under curve) after an oral dose/AUC after IV dose
- Low F caused by poor absorption, or extensive metabolism in the gut wall or liver

Absorption

- 3 routes
 - Passive diffusion:
 - Most important
 - Net transfer depends on concentration gradient and lipid:water partition co-efficient
 - Lipid soluble drugs absorbed more quickly
 - Non-ionised drugs absorbed quicker (more lipid soluble)
 - Absorbed along whole GI tract: basis for slow release preparations

- Active transport: highly specific – usually for transporting naturally occurring substances (e.g. amino acids)
- Filtration through pores: absorbed via paracellular route in small intestine. E.g. frusemide, atenolol, digoxin
- Factors affecting oral absorption:
 - Formulation: affects solubility and bioavailability. Presence of other drugs (e.g. Fe, Ca)
 - Gastric emptying: ↓emptying → ↓ absorption rate
 - Food: may slow gastric emptying, alter ionisation, decrease first pass metabolism. Affects different drugs differently
- Alternative sites of absorption:
 - Plasma concentration rises quickest for iv > im > sc (absorption similar to im but ↓ blood supply)
 - Intramuscular injection: affected by lipid solubility and blood flow
 - Rectal absorption: avoids GI irritation, good in vomiting, doesn't avoid 1st pass metabolism
 - Pulmonary absorption: small particle size
 - Absorption from mouth: nitrates/buprenorphine
 - Absorption from nose: desmopressin & other peptides
 - Percutaneous: zero order absorption – for nicotine, nitrates, scopolamine

Distribution

- Drug can be bound or unbound in both plasma and tissues
- Drugs bind to albumin (acidic drugs), α1 acid glycoprotein (basic drugs), tissue proteins
- Lipid solubility:
 - Penetrate lipid membranes easily (e.g. placenta, blood/brain barrier)
 - Rapidly distributed, dissolves in fat → plasma levels fall quickly, and large volume of distribution
 - Is non-polar or unionised
- Water soluble:
 - Excreted by kidneys (some also metabolised by liver)
 - Redistributions in water, smaller volume of distribution
- Ionisation of acid or base:
 - Depends on pH and pKa (the pH at which 50% of drug is ionised)
 - As pH ↑ (becomes more alkaline) an acid becomes more ionised, and a base less ionised
 - Only unionised drug will diffuse across lipid membrane

Metabolism

- Water soluble: excreted unchanged through the kidney
- Lipid soluble: Can't be excreted by kidneys (reabsorbed straight away) so conjugated or metabolised → water soluble → excretion
- Metabolism:
 - May result in activation of a pro-drug, active metabolites or inactive metabolites
 - Phase 1: oxidation, reduction, hydrolysis
 - Phase 2: conjugation, eg methylation, acetylation, glutamine, etc
 - Occurs mainly in the liver, also in the lung, kidney, blood, small intestine, gut bacteria
- 1st pass metabolism: high > 70%, e.g. lignocaine, GTN (no use taking them orally)
- Examples of drug metabolic reactions:

Reaction	Substrates
Cytochrome P450 (oxidation)	Many drugs, carcinogens
Oxidation of alcohols/aldehydes	Ethanol
Oxidation of purines	Azathioprine
Oxidation by MAO	Tyramine, catecholamines
Hydrolysis	Suxamethonium
Acetylation	Dapsone
Glucuronidation	Phenols, morphine

- Factors affecting metabolism: genetics, ethnicity, age, gender, pregnancy, liver disease, time of day, environment, diet, malnutrition, alcohol, other drugs

Excretion of Drugs

- Excretion:
 - Major routes renal, hepatobiliary, pulmonary
 - Minor routes: saliva, breast milk, tears

- Renal:
 - Few are excreted unchanged. Lipid soluble undergo tubular reabsorption
 - Only unbound particles excreted \Rightarrow if highly bound then slower excretion
 - Some are secreted by active tubular secretion e.g. penicillin, digoxin
 - Urine pH: alkaline urine \rightarrow \uparrow weak acid excretion (eg salicylates) and visa versa
- Biliary:
 - Polar drugs likely to be excreted in bile, e.g. rifampicin, ampicillin
 - Some drugs undergo entero-hepatic circulation, e.g. oestrogens

Inter-individual Differences

- There are large inter-individual differences in the capacity to metabolise drugs, due to:

Genetic factors

- Characteristics can be autosomal dominant, autosomal recessive, sex-linked, etc
- Either polygenic or monogenic (present either as polymorphisms – more than 1% - or as rare phenotypes - <1 %)
- Cytochrome P450: a group of enzymes located on the endoplasmic reticulum. Divided into families and sub-families
- 3 polymorphisms have been well defined:
 - Acetylation: enzyme: n-acetyl-transferase 2. Leads to slow and fast acetylators. 90% of Japanese are fast acetylators (autosomal dominant) compared with 55 – 60% of Europeans who are slow acetylators. Affects eg isoniazid and caffeine
 - Oxidation: poor metabolisers are deficient in enzyme CYP2D6, affects 4 hydroxylation pathway. Covers lots of drugs – TCAs, antipsychotics (e.g. haloperidol), β blockers (e.g. metoprolol). \uparrow Risk of accumulation. Rest of population are extensive metabolisers
 - Oxidation (CYP2C19): affects diazepam, omeprazole, others

Disease

- Absorption in disease:
 - Can affect gastric emptying rate: affects rate not extent
 - \downarrow Absorption rate in migraine, acute MI, labour, malabsorption syndromes (variable effect)
 - Low cardiac output \rightarrow \downarrow IM absorption
- Distribution:
 - For drugs with low Vd and high binding (only), changes in protein binding: e.g. \downarrow albumin in hepatic disease, nephrotic syndrome, \uparrow α 1AGP in RA, Crohn's. Amount of free drug is the same. But normally total plasma concentration measured (and this will be reduced) \rightarrow danger of overdose
 - Cardiac disease \rightarrow altered distribution (eg due to reduced gut flow \rightarrow poor absorption, \downarrow renal and hepatic perfusion \rightarrow \downarrow clearance)
 - Obesity \rightarrow increased Vd for lipophilic drugs
- Metabolism:
 - Most biotransformation occurs in liver. For some drugs, extraction depends on blood flow (where extraction ratio tends to 1)
 - Liver disease \rightarrow \downarrow capacity of metabolising enzymes (eg \uparrow warfarin, phenytoin) and possibly shunting of blood around liver (affects drugs with high first pass metabolism)
 - Thyroid diseases \rightarrow \uparrow or \downarrow metabolism
 - Diabetes mellitus \rightarrow fatty liver \rightarrow change in metabolism
 - Low clearance with high (>90%) degree of protein binding – generally \downarrow clearance
 - Low clearance, low binding (e.g. paracetamol) – variable but can be \downarrow clearance
- Excretion:
 - For many drugs, reduction in clearance \rightarrow \uparrow half-life
 - Adjust dose using creatinine clearance formula: Cockcroft Gault Formula (a prediction which saves doing a 24 hr urine):

$$\text{Cr.Cl ml/sec} = \frac{(140 - \text{age}) * \text{wt(kg)}}{50,000 * \text{serum Cr (mmol/L)}}$$

- Normal is 1.5 mls/sec. For mls/min, replace 50,000 by 815
- For females, multiply by 0.85

- Important for eg digoxin and aminoglycosides which are excreted unchanged. If elderly → ↓excretion → ↑plasma concentration
- Dose rate for a drug excreted 100% by the kidney (e.g. antibiotics) is:

$$DR = (Cr.Cl / 1.5) * \text{normal DR}$$

- This dose requires adjustment when not all the drug is excreted unchanged.

$$DR = (1 - fu) + fu * Cr.Cl / 1.5 * DR$$

Fu = fraction excreted unchanged

- Liver disease: arbitrary rule:
 - ↓Dose by 50% for high clearance drugs (high 1st pass metabolism)
 - ↓Dose by 25% for low clearance drugs (enzyme capacity only)
- Dosing in CV disease:
 - ↓Vd (vasoconstriction)
 - ↓Renal flow → ↓excretion
 - ↓Mesenteric blood flow → ↓absorption of frusemide

Age

- Epidemiology:
 - Elderly > 75 years
 - More likely to have multiple drugs (median per person over 65 is 3), 90% have one drug
 - 2 * incidence of adverse reactions (20 – 25%). ↑ in proportion to number of drugs
 - 30% of elderly admissions due to drug problems
- Absorption: little difference compared with young, except if other drugs interfere (eg ↓ transit time)
- Distribution:
 - ↓Lean body weight. ↑Vd of fat soluble drugs (eg diazepam), possible problems with accumulation
 - May be ↑adipose compared with lean body tissue. Eg smaller loading dose of drugs with low Vd (eg digoxin and cimetidine)
 - Protein binding: Albumin declines with age → significant change only in tightly bound drugs (ie small Vd, eg phenytoin) or zero order elimination (eg warfarin)
- Metabolism: Hepatic clearance:
 - Liver has significant residual capacity so not much decline with age, especially given ↓lean body weight
 - But significant (50%) reduction in liver blood flow, so significant reduction in metabolism of 1st pass metabolism (eg propranolol) or capacity limited metabolism (phenytoin or theophylline). Problem if narrow TI
 - ↓Hepatic blood flow and hepatic mass
 - ↓First pass clearance: eg major tranquillisers, TCAs, antiarrhythmics
- Excretion:
 - Decline in renal function. ↓GRF by 50% (although wider spread of function → ↑inter-individual variability). Problems with digoxin, lithium and gentamycin
 - ↓Renal clearance (see creatinine clearance above). However, ↑variability in serum creatinine (eg proportional to lean body mass) → less reliable estimate of renal function
 - Delayed action of renal acting drugs (eg diuretics)
 - Tolerate renal side effects less well (eg NSAIDs)
 - Need to adjust dose of: digoxin, cimetidine, ACE inhibitors, NSAID, Diazepam, aminoglycosides.

$$\text{Dose adjustment factor} = \frac{1}{F(Fk - 1) + 1}$$

- F = fraction of drug normally excreted unchanged
- Kf = relative renal function of a patient =
 - actual or derived Cr clearance [use Cockcroft & Gault formula]
 - normal Cr clearance

- Principles of geriatric prescribing:
 - Full drug history
 - Reasonable therapeutic objective (ie forget management of long term risk factors if they're 95)

- Individual dose titration – beware ‘usual’ doses
- Lowest possible dose
- Simplest possible regime
- Regular review of drug therapy

Children

- Clearance: functional maturity reached from 6 months to 1 year
- Vd: have more body water and less fat \Rightarrow \uparrow dose for H₂O soluble and \downarrow for lipid soluble
- Guidelines:
 - If < 6 months: consult a paediatrician
 - 6 months to 1 year: use a nomogram for surface area. Estimates Dose = [wt (kg) $^{2/1.7}$ m 2] * adult dose

Other Factors

- Sex: Women clear BZDs faster, NSAIDs slower
- Pregnancy: more rapid clearance of oxidised drugs due to \uparrow liver flow. See Pharmacology of Pregnancy and Breast Feeding, page 528
- Obesity: Use ideal body weight if actual > 30% above ideal for drugs with low Vd
- Environment
- Diet: eg smoking, grapefruit juice, malnutrition, alcohol

Controlled Release Formulations

- Aim is to prolong short acting drugs, to reduce daily dose frequency
- Also a drug company ploy: introduce slow release formulation to extend patent
- Good points:
 - Increased compliance
 - \downarrow Side effects (but probably also decreased therapeutic effects)
- But:
 - Often more variability in plasma fluctuation. Eg Slower absorption + variations in 1st pass metabolism \rightarrow wider variation in clinical effect
 - Effect of variation in gastric emptying reduced
 - Adhesive patches cause skin reaction in 30%
 - Fixed dose: harder to titrate
 - \uparrow Cost

Pharmacodynamics

- =Study of drug/receptor interactions. Dimensions of time, concentration and effect (ie response intensity)
- Types of ‘receptors’ for drugs: enzymes, ion channels, receptors, carrier molecules. Most common targets are transmembrane receptors linked to G proteins
- Receptor interactions:
 - Agonists:
 - Bind and produce a full effect
 - Partial agonists: bind and produce sub-maximal effect (ie lower dose-response curve)
 - Inverse agonists: bind and have opposite effect to that of agonists
 - Non-competitive agonists cannot be displaced
 - Competitive agonists reversibly interact, can be reversed by an antagonist.
 - Antagonists: bind and produce no effect.
 - Competitive: maximal response is still possible with an \uparrow in dose of endogenous agonist (ie dose response curve shifts right). Eg \uparrow adrenaline can over-ride β -blockers
 - Non-competitive: don’t allow a maximal response regardless (ie lower-dose response curve). Progressively lowers maximal response of agonist
 - Agonist antagonist: has an agonist effect at one subtype of receptor and an antagonist effect at another
 - Specificity = effect produced by interaction with a single receptor
 - Ka = concentration required to occupy 50% of receptor sites at equilibrium
 - Up-regulation/down-regulation: a very common response to an antagonist/agonist. Watch for rebound when it stops

- Dose response curves:
 - Relationship between plasma concentration and drug's effect
 - Efficacy: maximal ceiling of effect, regardless of dose. Effectiveness of drug once bound to a receptor
 - Potency: quantity required for maximal effect
 - Affinity: if a drug has lower affinity, it can still produce a maximal effect but will require a larger dose (ie pushes dose response curve to the right). Higher affinity \Rightarrow higher potency.
 - Individuals vary considerably in the efficacy, slope (difference between small and maximal effect) and potency of drugs. Eg with \uparrow age have \downarrow receptors. So dependent on age, disease, environment, etc
- Concentration vs. response:
 - EC50 = drug concentration at 50% of maximal effect (describes affinity of the drug for the receptor)
 - Therapeutic index is the ratio of the Adverse Effect EC50 to the Therapeutic Effect EC 50
 - Rise in response intensity is normally less than proportional to drug concentration. It reaches a point where further increases in concentration have no further effect (but may prolong effect – but to double time may need 10 fold \uparrow in concentration). Need to balance against \uparrow adverse effects
 - Usually presented as Response vs log drug concentration – this linearises the central part of the curve
 - Combining with another drug with a synergistic effect changes the dose response – often allows \downarrow dose (eg ACE + diuretic)
- Dosing:
 - 'Usual dose': set at maximum profit for minimum toxicity. Always half New Ethicals starting dose!
 - Objective in chronic disease management: use the lowest possible daily dose of the appropriate drug. Building up slowly, but this is usually impractical in general practice (requires lots of visits until therapeutic effect satisfactory, so back titration used)
 - Loading dose dependent on volume of distribution
 - Infusion rate dependent on clearance
 - Constant infusion \rightarrow gradually rising Cp. Bolus \rightarrow instantly high Cp, then declining. Both \rightarrow stable Cp
- Factors in Failure to respond:
 - Poor compliance: difficult dosage regimes, poor technique (eg inhalers), difficult to swallow, etc. Frequency critical. Increasing frequency \rightarrow more forgotten. But if $T_{1/2} < 24$ hours, will get better overall control (avoiding peaks and troughs in Cp) with $>$ once a day
 - Incorrect drug formulation
 - Altered drug handling due to disease state (eg impaired absorption of oral frusemide due to mucosal oedema)
 - Drug tolerance or bacterial resistance
 - Disease state too severe (eg thiazide diuretic in heart failure)
 - Toxicity may prevent attainment of the therapeutic dose

Changes with Age

- Blunted homeostatic reserve:
 - \uparrow Risk of postural hypotension with antihypertensives, neuroleptics, TCAs
 - Drugs have greater effect on postural control (eg sedatives)
 - Changes in neurotransmitters \rightarrow \uparrow risk of drug induced confusion
- Receptor changes. Eg \downarrow response to β agonists and antagonists

Pharmacology of Pregnancy and Breast Feeding

Pregnancy

- Risks are often unknown – although usually small
- Rule of thumb: DON'T use drugs in pregnancy
- Most drug induced abnormalities are subtle \rightarrow don't make link with drug
- Effects of harmful drugs:
 - Gametes \rightarrow sterility
 - Blastocyst \rightarrow death

- Embryo → death or major abnormality (heart, limbs, brain, eye form during embryogenesis)
- Fetus → Functional abnormality
- Factors affecting dysmorphogenesis:
 - Critical dose
 - Timing of dose during development
 - Fetal susceptibility
 - Fetal environment (eg already at risk due to diabetes, smoking etc)
 - Placental drug transfer: all drugs get across but in widely varying amounts. Lipid drugs with polar metabolites are bad news (drug crosses in, but metabolites can't get out, eg diazepam)
- Testing safety:
 - Validity of drug models
 - RCTs assess efficacy not safety
 - Can only pick them up with post-market monitoring and careful evaluation in clinical practice
- Effects of pregnancy on drug handling:
 - 30 – 50% delay in gastric emptying
 - Minimal effect on absorption
 - Albumin reduced by 25% by 15 weeks
 - Plasma volume increases by 50%
 - Total body water ↑ by 8 litres
 - 50% ↑ in renal blood flow
- Fetal renal excretion:
 - Fetal kidney's are functionally immature ($\text{Cr} = 2 - 4 \text{ mls at term}$ – very small)
 - Renal blood flow only 5% of cardiac output (25% in adult)
 - Renal elimination not an important route of drug metabolism (baby swallows it again anyway)
- Hepatic metabolism:
 - Shunt 30 – 70% of umbilical blood flow (ductus venosus)
 - Oxygenation of the Left lobe (umbilical vein) > than right lobe (portal vein)
 - Slower metabolic rate than adult but extensive CYP450 metabolism

Breast Feeding

- Transfer affected by:
 - PKa: Base transfers more as pH of milk is lower than blood
 - Lipid solubility
 - Molecular weight (eg high molecular weight heparin doesn't cross)
- Avoid:
 - Excess alcohol
 - Anticoagulants except heparin
 - Anti-thyroid drugs
 - Antibiotics: chloramphenicol, tetracyclines (affect teeth and growth plates), sulphonamides and quinolones
 - β-blockers: atenolol, sotalol → bradycardia. Other antihypertensives OK
 - Diazepam
 - Lithium
 - Combined OCPs
 - Anti-metabolic agents
 - Ergot derivatives (eg anti-migraine medication)
 - ?Diuretics
 - ?SSRIs
 - Phenytoin
 - NSAIDs – effect breast milk production

Adverse Drug Reactions (ADR)

- WHO definition: any response to a drug which is undesirable and unintended, and which occurs at doses used in man, for prophylaxis, diagnosis or therapy, excluding therapeutic failure
- Responsibility of prescriber is to observe, record and report adverse drug effects and interactions
- Includes:
 - Side effects
 - Intolerance (side effects occurring at levels normally well tolerated)

- Anaphylaxis
- Interactions with other drugs (e.g. pharmacokinetic reaction due to enzyme induction)
- Classification: includes mistakes (knowledge based errors) and lapses (skill based error)
- Grading them:
 - Serious: results in death, hospitalisation or persistent disability
 - Severity: intensity of reaction not seriousness of reaction (ie a severe skin reaction may not be serious)
- Incidence:
 - True incidence unknown
 - Estimated 3 – 5 % of all hospitalisations due to an ADR
 - Estimated 3 in 1000 hospital deaths due to a drug reaction
 - Common in elderly
- Monitoring:
 - Medicine Assessment Advisory Committee reviews new drugs prior to licensing
 - Can be licensed for monitored use through the Intensified Medicines Monitoring Programme (IMMP). Requires reporting of ALL new clinical events in a patient
 - Voluntary reporting to the Centre for Adverse Reactions Monitoring in Dunedin (reporting rate estimated < 15%)
 - Danger/Warning Notification System with NHI number. Records potentially life-threatening reactions
- Difficulties in recognising ADRs:
 - May mimic a common symptom (eg headache)
 - May be so bizarre that a common drug escapes suspicion
 - May be a long delay (eg hepatotoxic reactions)
 - The ADR may be confused with the disease (eg antibiotic fever in meningitis)
- Recognising an ADR: suspicion, how often does this occur without the drug (ie reference rate of the disorder), temporal sequence, what happens when drug is discontinued and/or rechallenged
- Frequency of effect:
 - Clinical trials are poor indicators of ADRs. Not sufficient numbers to find rare effects, so post market surveillance important
 - Eg:

	GI bleed	Agranulocytosis
Reference Rate	1:100	1:100,000
Rate with NSAID	5:100	5:100,000
Rate Ratio	5	5
Attributable Fraction	80%	80%
- Determinants of ADRs:
 - The drug itself: rate, route, formulation, dose
 - The patient:
 - Age: young (immature conjugating enzymes) and elderly (\downarrow clearance)
 - Gender: more common in women. ?Effect of sex hormones, ?less gastric acid, compounding effect of \uparrow health seeking behaviour
 - Disease: diseases of heart, kidneys, liver all affect drug kinetics and dynamics. Eg, AIDS \rightarrow \uparrow risk of ADR with co-trimoxazole
 - Previous history: Previous reaction \rightarrow \uparrow risk
 - Genetic and ethnic factors, eg altered rates of metabolism
 - Extrinsic factors:
 - Alcohol consumption, tobacco, pollutants
 - Multiple drug therapy: 1 – 5 drugs \rightarrow 3.3% risk, 6+ drugs \rightarrow 19.8% risks
- Mechanisms of ADRs:
 - Type A – predictable.
 - Exaggerated primary therapeutic effects. Risk is increased with \uparrow dose or \downarrow clearance. Rarely serious. Eg anticoagulants \rightarrow bleeding, hypotension with antihypertensives
 - Primary drug effects that are not therapeutic. Eg β blockers \rightarrow bronchospasm
 - Type B - unpredictable. Dose independent, low incidence, serious. Eg anaphylaxis to penicillins, carcinogenicity, dental discolouration from tetracyclines

Drug Allergy

- = Specifically altered potential reactivity to a drug or breakdown product of a drug

- Recognition of an allergic drug reaction:
 - Always a delay in allergic reaction following initial exposure
 - Once established, a reaction can be precipitated by minute amounts of the drug
 - There is recurrence on re-exposure
 - The reaction doesn't resemble the pharmacological activity of the drug
 - Symptoms suggest an allergic response
- Four main mechanisms for inducing an immunotoxic reaction:
 - Drug may be an immunogenic protein
 - Drug or metabolite may form a haptene by combining with endogenous proteins
 - Drug/metabolite may cause a reaction between a modified self-antigen and an antibody
 - Drug/metabolite may cause the synthesis of auto-antibodies, but its continued presence is not required for binding between the antibody and the antigen
- Four types of reaction (Coombs-Gell types): (See Allergy and Hypersensitivity Disorders, page 309)
 - Type 1 (immediate) hypersensitivity: Drug or drug conjugate binds a specific IgE on the surface of basophils and mast cells → degranulation → mediator release → bronchospasm, urticaria, anaphylaxis
 - Type 2 (cytotoxic) hypersensitivity: IgG or IgM + drug-protein conjugate → complement release → complement activation → haemolysis or neutropenia or thrombocytopenia (depends on which cell surface reaction takes place). Eg quinine
 - Type 3 (immune complex) hypersensitivity: (actually rare) protein complexes + IgG → insoluble matrices → complement activation → localised vascular damage with Serum Sickness/Antibiotic Fever (fever, joint pain, lymphadenopathy, neutropenia, glomerulonephritis). Eg Presents 1 – 3 weeks after penicillin/cephalosporin/sulphonamide treatment.
 - Type 4: (delayed) hypersensitivity (cell mediated): drug-protein complex + target cell → recognised by T-lymphocyte → direct cytotoxicity/macrophage activation. Eg contact dermatitis due to chlorpromazine
- Symptoms:
 - Localised: urticaria (weals, always itch), bronchospasm, angioedema
 - Generalised: hypotension, bronchospasm, urticaria, laryngeal oedema
- Examples:
 - Haemolytic anaemia: eg levodopa, captopril (ACE inhibitor), penicillins
 - SLE: eg phenytoin, gold, procainamide (antiarrhythmic)
 - Glomerulonephritis: eg gold, drugs with sulphydryl group
 - Aplastic anaemia: eg phenytoin
- Factors influencing occurrence of allergic reactions
 - Duration and the number of courses or treatment
 - Any route (although anaphylaxis more common with iv)
 - IV anaphylaxis occurs with the same frequency in the general population and atopic individuals. Anaphylaxis by other routes more common in atopic individuals
 - More common in adults than children (?less exposure to drug antigens)
 - Previous history of any allergic reactions and co-existing disease states

Drug Interactions

- = Effects of one drug are increased or decreased by another
- Lots of interactions: the key is their significance
- Often caused by Polypharmacy:
 - = "Irrational concurrent use of several different drugs"
 - Common in:
 - Multiple medical problems
 - Long term care
 - "Standing orders", sedatives, laxatives, antidiarrhoeals, cough medicine
- Guide to potential drug interactions:
 - How commonly are interacting drugs used together?
 - Does one of the drugs have a low TI? Eg probenecid reduces penicillin clearance, but who cares. Erythromycin reduces theophylline clearance – critical
 - Has a potential interaction been validated in in-vivo studies?
 - Are there case reports of adverse effects?
 - Is there a reasonable mechanism for the interaction?

- Risk factors for drug interactions:
 - Low volume of distribution (V_d) → ↑ plasma concentration (esp if protein bound)
 - Narrow TI (toxicity with small changes)
 - Capacity limited hepatic clearance (cf blood flow limited), eg phenytoin
 - Extensive Metabolisers (EM): those genetically predisposed to rapid metabolism. Add in an enzyme inhibitor → more dramatic change
 - High protein binding (→↑↑ plasma concentration if protein binding disrupted)
 - Acidic drugs: readily displace basic drugs
 - Active renal tubular excretion (other drugs can compete for excretion pathways → ↓clearance)
 - IV administration (risk of mixing drugs that shouldn't be mixed)
- Pharmacokinetic mechanisms:
 - *Drug Inactivation:* Eg Cholestyramine (ion binding resin) binds oral anticoagulants
 - *Altered absorption:* Metoclopramide (↑gastric emptying) + digoxin (takes long time to breakdown in stomach) → ↓ absorption. Metoclopramide + paracetamol → faster absorption
 - *Protein binding:* Adverse reactions do not occur purely because of displacement from protein binding sites: Eg phenytoin + hypoalbuminaemia → ↓ binding → ↑clearance → ↓total concentration → ↑free fraction but free concentration remains the same
 - *Drug excretion:* Probenecid + Penicillin – competition for limited capacity of active tubular excretion. Diuretics → ↓ Lithium clearance
 - *Drug metabolism:* Metabolic reactions are unpredictable and highly variable.
 - Multiple Cytochrome P450 enzyme phenotypes, each with its own selectivity for inhibitors (immediate effect) or inducers (takes weeks, requires transcription, etc). Eg sulphapyrazone: inhibits tolbutamide, warfarin, and phenytoin. Induces theophylline and verapamil
 - CYP450: Mixed function oxidase system. Genetic polymorphism results in:
 - Extensive metabolisers (EM). Inhibition reactions will convert these to PMs
 - Poor metabolisers (PM). Inhibition reactions won't affect these
 - Ultra-rapid metabolisers (eg CYP2D6). Marked differences in genetic polymorphism (eg CYP2D6 – 7% Caucasian, 1% Asian)
 - Inhibition of CYP450 → ↑risk of type A reaction to another drug metabolised by the same enzyme
 - CYP3A4 is the most abundant P450 enzyme (metabolises over half of all drugs):
 - Induced by carbamazepine, rifampicin, dexamethasone
 - Inhibited by grapefruit juice, azole antifungals, erythromycin
 - Enzyme inducers: chronic ethanol, anticonvulsants, rifampicin, isoniazid (Tb antibiotic)
 - Enzyme inhibitors: acute ethanol, ANTIBIOTICS: macrolides (eg erythromycin), metronidazole, sulphonamides, quinolones (eg ciprofloxacin), azole antifungals, cimitidine, MAOIs, SSRIs, amiodarone, verapamil, omeprazole, grapefruit juice (inhibits CYP3A4)
 - Eg non-sedating anti-histamines (eg terfenadine / Teldane). Concentration dependent inhibition of K⁺ influx → prolongs action potential → ↑QT interval → torsade de pointes → sudden death (very rare). However, ↑Cp due to CYP450 inhibitors (eg erythromycin, cimetidine) → ↑risk of sudden death
- Pharmacodynamic mechanisms:
 - = Additive or opposing effects at the same or different receptors
 - Majority of drug effects
 - Examples:
 - Combinations of agonists or antagonists at the same receptors: eg Anxiolytics (lorazepam) + hypnotic (triazolam) → ↑BDZ adverse effects
 - Combinations of agonists and antagonists: eg phenothiazine + L-Dope = antagonism of anti-parkinsonian effect
 - Combinations of agonists or antagonists at different receptors: eg ethanol + benzodiazepines → ↑sedation
- Pharmaceutic mechanisms: the interaction occurs prior to systemic availability
- Common examples:
 - Ethanol/drug interactions:
 - CNS depressants: alcoholics need more to sedate but stay under longer
 - Anticonvulsants: unpredictable
 - Metronidazole gives a disulfiram reaction (Antabuse)
 - Warfarin: acute ethanol inhibits metabolism, chronic ethanol induces metabolism

- Antihypertensives have decreased effect
- Oral contraceptives:
 - 23% of OC failures associated with antibiotics
 - Mid cycle breakthrough bleeding may indicate important antibiotic effect (\downarrow oestrogen level)
 - Should have alternative contraception for the antibiotic course and 7 days afterwards with no pill free period. No action required for stat antibiotic doses or POPs
 - Other interactions: antacids, H2 antagonists, NSAIDs, cough and cold remedies (pseudoephedrine)

Therapeutic Drug Monitoring (TDM)

- Used to titrate the ‘usual dose’ to an individual
- Monitoring Cp (plasma concentration) assumes no receptor tolerance, accurate determination of the biological effect and accurate determination of the plasma level
- Indications for TDM:
 - Availability of an accurate, precise, specific and inexpensive test
 - Long term drug therapy where clinical definition of efficacy is difficult (ie won’t know if it’s working by observing the patient)
 - Dose related adverse effects for which there are few clinical warning signs/symptoms
 - Substantial inter- and intra-individual variability in pharmacokinetics
 - Multiple drug interactions
 - Drugs with a narrow therapeutic index: phenytoin, digoxin, theophylline, lithium, gentamicin
 - Suspected non-compliance
 - Unexpected lack of response or signs of toxicity
 - But TDM should not replace clinical judgement
- Therapeutic index: top and bottom are blurred margins/probabilities
- Blood sampling for TDM:
 - Often done badly
 - When absorption and distribution phases are complete
 - Steady state plasma conc. (5 half lives after started)
 - Sample just prior to next dose when dosing $2 * T\frac{1}{2}$. Sample 3 – 5 hours post dose for slow release formulations
- Examples:
 - Phenytoin: Has dose dependent kinetics. Dose changes should not exceed 20% of total daily dose. Metabolised by CYP450 with many interactions. CNS toxicity correlates well with blood concentrations (nystagmus, ataxia, atypical convulsions). Therapeutic concentrations controversial (based on studies in severe epileptics). Reduce in hypoalbuminaemia (Same dose $\rightarrow \downarrow$ binding available $\rightarrow \uparrow$ free conc.) Frequent error: sample in trough of plasma concentration – then appears to be below TI
 - Lithium: narrow TI for maintenance – 0.4 – 0.8 mmol/L. Minor symptoms (eg tremour, nausea) don’t predict serious toxicity. Renal clearance \downarrow by diuretics, theophylline, caffeine, dehydration, low sodium diet. TDM mandatory when side effect, relapse, serious illness, dose adjustment. 3 monthly monitoring for Li levels, electrolytes, thyroid fn
 - Theophylline (bronchodilator): Dose related toxicity: seizures, arrhythmias. Elimination reduced with erythromycin, ciprofloxacin, cimetidine, smoking cessation, hypothyroidism (all \downarrow P450)
 - Digoxin: variable bioavailability (eg with cholesterol binding agents, antacids) and large variability of clearance (\downarrow with NSAIDs, spironolactone, verapamil, amiodarone). \uparrow Effect in hypokalaemia, hypothyroidism, elderly. \downarrow Effect in hyperthyroidism and pregnancy. Sample 8 – 12 hours post dose (long distribution phase).
 - Aminoglycosides: Dose predictions performed by pharmacy

Poisoning and Drug Overdose

- See Poisoning and Overdose, page 488

Drug withdrawal syndromes

- Alcohol: tremor, sweats, tachycardia, \uparrow BP, seizures, visual hallucinations, delirium
- Opioids: anxiety, lacrimation, fever, runny nose, muscle aches, nausea, vomiting, diarrhoea, dilated pupils, tachycardia. Give naloxone for overdose (give test dose first, in case its not opiates). Pentazocine and Buprenorphine also used

- BZD Withdrawal:
 - Anxiety, insomnia, depersonalisation, perceptual disorders, tremor, maybe seizures and confusion
 - Usually short acting (long acting less likely to give withdrawal affects)
 - Eg Triazolam: rebound wakefulness (can last 4 – 7 days). Also behavioural disinhibition, amnesia, confusion, etc
 - If severe then weight loss, autonomic dysfunction, ↓BP, ↑↓ temp, tachycardia, psychosis, seizures. Have to restart drug and withdraw slowly
- Propranolol withdrawal:
 - All β blockers can do it: but more common with short acting (eg propranolol and metoprolol). Less common with long acting (atenolol) or slow release
 - On withdrawal, sympathetic activity overshoots due to receptor up-regulation while on drug
 - Palpitations, sweating, apprehension, arrhythmias, etc. Peak is 3 – 5 days following withdrawal, especially with physical activity
- Clonidine withdrawal:
 - Antihypertensive. Pre-synaptic α₂ agonists → inhibits nor-adrenaline release
 - Withdrawal in 10% → sudden rise in BP 24 – 72 hours later, plus other sympathetic effects
 - Similar effect in methyldopa (antihypertensive used in pregnancy)
- Diuretics: eg frusemide, thiazides. ↑Na retention over 4 – 5 days. Returns to normal
- TCAs, phenothiazines, butyrophenones: headache, nausea, vomiting, confusion in elderly. Sleep disturbance

Sleep

- Changes in elderly sleep patterns:
 - Sleep latency unchanged (= ability to get off to sleep)
 - ↑Stage 1 and 2 sleep (light sleep) – effects early morning
 - ↓Deep sleep and REM sleep
 - ↑↑Wakefulness
- For elderly, less sleep is a normal physiological process – they're sleeping the amount they need. Problem is often anxiety about and during wakefulness

Treatment of Insomnia

- A distressing complaint – not an illness
- Normal aging increases wakefulness during last 4 hours of sleep (reassure patient insomnia is ‘normal’)
- Non-drug management:
 - First check for: anxiety, depression, comfort, incontinence (eg diuretics), dementia, and treat these
 - Obtain careful sleep history, note factors improving/worsening sleep
 - Good explanation
 - Good Sleep Habits (Sleep Hygiene):
 - Reduce light, noise and extremes of temperature
 - Ensure physical security
 - Avoid caffeine, nicotine and alcohol before bedtime
 - No heavy meal for 2 hours beforehand, but have a light snack if hungry
 - Regular exercise last in the afternoon/early evening, but nothing vigorous for 3 hours beforehand
 - Allow one hour of quiet activity before bedtime (reading, TV, music)
 - Develop a bedtime ritual, cleaning teeth, reading, etc
 - Don’t go too early (ie before you feel sleepy)
 - Don’t stay in bed if you are awake. If not asleep within 15 – 20 minutes (estimate – don’t use a clock), get up, go elsewhere and do something mundane until you feel sleepy again
 - Get up at the same time in the morning: don’t sleep in on weekends or after late nights. This helps train your body clock
 - Don’t nap during the day
 - Don’t worry if you can’t get to sleep at night: worry will delay sleep even more
- Drug management:
 - 30% over 65 take sleeping pills
 - Not for persistent insomnia (common in personality disorders, depression, sleep apnoea, pain, gastro-oesophageal reflux – treat primary cause).

- Hypnotics should only be prescribed for symptomatic temporary insomnia (no more than 2 – 3 weeks) and should only be part of an overall management strategy
- If used, for defined period, perhaps intermittently, and should sustain sleep
- Not:
 - Short acting (eg midazolam) get them off to sleep – but don't sustain sleep. Don't have any impact on early morning wakefulness. So will wake, and take another – then hangover in the morning, ↑falls, etc
 - Long acting (triazolam/Halcyon) - which leads to daytime anxiety
- Use intermediate-acting hypnotics (eg zopiclone and temazepam)
- Risk of addiction
- Shift workers should avoid them

Compliance Issues

- Compliance = extent to which person's behaviour coincides with medical advice
- Few people take their medication as prescribed
- Non-compliance is multi-factorial:
 - Rapport with doctor
 - Not knowing how to take medication
 - Not understanding the importance of the drugs
 - Taking many drugs
 - Anticipation or experience of side-effects
 - Forgetfulness
 - Impaired physical function or other disability
 - Community and family support
- Strategies for improving compliance:
 - Education about disease and treatments (spoken instructions are quickly forgotten)
 - Simplifying drug regimes (fewer drugs and fewer doses)
 - Involving carers
 - Education about common side effects which may subside
 - Use of drug diaries, calendars, medication charts
 - Use of ordinary bottle tops (not childproof) for elderly people
 - Large print labels
 - Dosage forms (eg small pill size, pleasant taste)
 - Compliance aids such as pill trays and blister packs
 - Return or destruction of old drugs

Prescribing

- Definition of a medicine:
 - Medicines Act 1981 and Medicines Regulations 1984
 - "Administered to one or more human beings for a therapeutic purpose":
 - Treating or preventing disease
 - Altering the shape, size, structure or weight of the human body
 - Cleaning, soaking or lubricating contact lenses
- Registered medicines:
 - Registered medicines are gazetted and approved by the Ministry of Health
 - Unregistered medicines can be used under section 29 – requires special consent process
 - Unregistered indication
- Classification of medicines:
 - Prescription medicines
 - Pharmacist only medicines (formerly restricted medicines)
 - Pharmacy medicines (formerly pharmacy only medicines)
 - General sales medicines
 - Controlled drug
- Legal requirements for all prescription types:
 - Legibly and indelibly printed
 - Signed personally by the prescriber and dated
 - Contain the address of the prescriber

- Contain the surname, initials and address of the patient
- If under 13, the child's date of birth
- Indicate the name and where appropriate the strength of the medicine
- Indicate the total quantity to be dispensed on each occasion
- Indicate the dose and frequency for medicines intended for internal use
- There are special script pads and requirements for controlled drugs (see the Preferred Medicines List)

Regulation of Medicines and Drugs

- Medicines Act 1981: prescription medicines can only be supplied or possessed on the prescription of a doctor and dispensed in a pharmacy. Maximum amount = 3 months supply (6 months for oral contraceptive)

Regulation of Drugs of Abuse

- See also Drugs of Abuse, page 448
- Misuse of Substances Act 1975 defines and regulates controlled drugs - prohibits non-therapeutic use. Mainly Opiates, Ritalin, dexamphetamine and BZDs
- Prescriptions for opiates and stimulant-controlled drugs must be on a special triplicate form in the Doctors own writing. BZDs don't require triplicate form
- Prescribed for maximum of one month, dispensed in 10 day lots
- It is illegal to supply a controlled drug for the treatment of maintenance of dependency (except for Gazetted drug clinics)
- Need good notes to avoid legal recourse (e.g. no automatic repeats)
- Many injected drugs have been prescribed 'legally' by doctors and diverted to illicit use (eg sold to dealers)
- Monitoring of prescription narcotics and abuse prone medicines is carried out by Medicines Control Advisors, reporting to the Medical Officer of Health
- They can issue a Restriction Notice – which prevents the supply of controlled or specified drugs to a named person – it is then an offence for this person to try and obtain this drugs, and a doctor to prescribe it for them

Classes of drugs

- Responsibilities of the prescriber:
 - To avoid creating dependence
 - To see that the patient doesn't increase the dose, inducing dependence
 - To avoid unwittingly supplying the black market
- Misuse of Substances Act:
 - Grades drugs according to harmfulness when misused. Specifies recording, reporting and form filling requirements. Enforced by Customs, Police (where criminal acts) and by Medical Officer of Health in the Ministry of Health
 - Class A: Possession, prescribing, sale are prohibited – street drugs. Use is an offence (e.g. heroin). Large penalties
 - Class B: Can only be used for pain. Can only be prescribed for dependency by a gazetted person. Includes morphine, methadone
 - Class C: Controlled drugs which are less hazardous (eg codeine, BDZs, etc)

Clinical Trials

- Preclinical trials: testing toxicity and potential therapeutic benefit
- Phase 1: Human pharmacology
- Phase 2: On patients – focus is safety: dose level and frequency, unwanted effects, treatment duration
- Phase 3: On more patients – designed to test efficacy not safety
- Medicines licensed for use
- Phase 4: Adverse reaction monitoring – rare effects only show up with widespread general use ⇒ big responsibility on prescribers to report ADR

MedSafe

- = NZ Medicines and Medical Devices Safety Authority. Part of the Ministry of Health.
- www.medsafe.govt.nz - has data sheets for all drugs
- Medicine = any substance ... supplied wholly or principally to treat a human for a therapeutic purpose
... treating or preventing a disease

- Medsafe regulates:
 - From production to distribution
 - Access to medicines (eg prescription, restricted, pharmacy only, general sales)
- Need to regulate to protect public health and to avoid counterfeit or inferior quality medicines

Anaesthetics

- References: Anaesthesia, Resuscitation and Emergency Management, Wellington School of Medicine, 2000
- See also Paediatric Anaesthetics, page 655

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General Anaesthesia

- Anaesthesia = absence of all sensation
- The reversible induction of:
 - Hypnosis
 - Autonomic reflex suppression
 - Muscle relaxation
- One drug doing all (e.g. inhalational anaesthetic such as isoflurane) would require sufficiently high doses to cause major side effects (e.g. respiratory depression, prolonged recovery)
- Balanced anaesthesia: one drug for each component → minimal homeostatic depression and quick recovery:
 - Hypnotic: e.g. thiopentone or halothane
 - Opiod: abolish autonomic response to painful stimuli
 - Muscle Relaxant
- Stages:
 - 1 – confusion
 - 2 – exaggerated reflexes, severe confusion
 - 3 – Light, surgical and deep anaesthesia
 - 4 – medullary paralysis
- With increasing depth there is:
 - Loss of reflexes causing cough and swallowing → aspiration
 - ↓ Muscle tone → airway obstruction
 - Progressive depression of ventilation
 - At deep level, medullary paralysis with apnoea and cardiovascular collapse
- Major problem is awareness if anaesthetic too light: anaesthetist won't know due to paralysis. Principal signs are stress responses: tachycardia, hypertension, mydriasis (large pupils), sweating, pallor. Additional hypnotic will remove consciousness of pain, additional opioid will suppress CNS reception of pain
- Monitoring:
 - ECG: heart rate, rhythm and ischaemia
 - Blood pressure: depressed by excessive depth, extensive local (e.g. spinal blocks), or blood loss, elevated by awareness, inadequate pain blockade or hypercarbia
 - End tidal CO₂: if ↑ then inadequate ventilation, if ↓ then excessive ventilation
 - Pulse oximeter: O₂ saturation
 - Temperature: anaesthetic agents → vasodilation → loss of temperature, also cold iv fluids
 - Muscle relaxation: neuromuscular block monitor
- Rapid Sequence Induction/Intubation: Intubation of someone not properly prepared for surgery (eg not fasted so risk of gastric aspiration/regurgitation). Drugs to paralyse (e.g. Suxamethonium – fast acting) and sedate (e.g. propofol). Press down on cricoid cartilage until intubated to stop aspiration (closes off oesophagus) – but not if actively vomiting (otherwise gastric or oesophageal rupture)

Anaesthetic Agents

Dose Calculations of Anaesthetic Drugs

- Concentrations. Four most common methods of specifying concentration are:
 - Mg/ml: weight of drug per volume of diluent
 - % - number of grams of drug per 100ml. E.g. 50% = 50 grams per 100 ml or 500 mg/ml. 1% = 10 mg/ml. Multiplying by 10 gives mg/ml. Often used for lignocaine (Xylocaine)
 - 1:1000 is the same as 0.1% (1 mg/ml). Used for adrenaline and isoprenaline
 - mmol/l: used for electrolytes
- Infusions:
 - Use for drugs with very short T_{1/2} where fluctuations in dose of drug are dangerous
 - Common for adrenaline, dopamine, dobutamine & lignocaine
 - E.g. post arrest infusion of lignocaine at 2 mg/min with 2% xylocaine. This is 20 mg/ml, so want 0.1 ml per minute. Using a burette system can deliver 6 drops a minute (60 drops = 1 ml) or dilute 10 fold and run at 60 drops per minute (easier)

Inhalational Anaesthetics

- Gases = compounds in the gaseous state at a temperature above their critical temperature.
- Vapours = compounds in gaseous phase but can be returned to liquid by ↑ in pressure. Ambient temperature must be below the critical temperature for the compound
- The partial pressure in the brain necessary to achieve anaesthesia will depend on its potency
- Poorly soluble gases will have higher partial pressure at a given concentration and will have a fast onset.
- Lipid soluble drugs are more potent
- So more soluble drugs have slower uptake in blood and require lower partial pressure to achieve their effect
- Factors affecting uptake:
 - Inspired partial pressure
 - Alveolar ventilation
 - Circulation
 - Properties of the anaesthetic agent (e.g. blood solubility)
- Nitrous Oxide (N₂O):
 - Pleasant, non-irritating, non-flammable (but supports combustion)
 - Stored in blue cylinders
 - Poorly soluble in tissues → rapid uptake and elimination
 - Good analgesic but low potency
 - Always given with at least 30% O₂ to avoid hypoxia
 - Expands in enclosed air spaces: so avoided for middle ear operations and where air embolism may occur
 - Give 100% O₂ at end of N₂O anaesthesia to avoid diffusion hypoxia – N₂O rapidly leaves pulmonary capillaries → ↓alveolar O₂ concentration
- Halothane:
 - High potency (Minimum Alveolar Concentration, MAC = 0.7% - level that produces immobility in 50% of people, NO₂ is 105% ⇒ not so good)
 - No irritation and moderately rapid induction and recovery
 - Poor relaxant and analgesic properties
 - Requires accurate vaporisers
 - High concentrations produce profound respiratory and cardiac depression
 - Rare complication is hepatic necrosis
- Isoflurane:
 - Similar to halothane, but more irritant so difficult to use for induction
 - More potent vasodilator → hypotension and tachycardia
 - Also sevoflurane: not so irritant, quicker onset, but more expensive. Use in kids if can't cannulate

Intravenous Anaesthetics

- Can be given as bolus for induction or infusion for maintenance
- All have similar characteristics:
 - All are lipid soluble
 - Unionised fraction crosses the blood brain barrier
 - Loss of consciousness usually occurs in one arm to brain circulation time (approx. 30 secs)
 - Rapidly redistributed to tissues with high blood flow so rapid fall in peak plasma concentration
- Thiopentone:
 - Barbiturate derivative containing sulphur (→ yellow)
 - Highly alkaline in solution → thrombophlebitis
 - Blood level results from distribution (seconds), redistribution (e.g. from muscle to fat – minutes/hours) and metabolism (15%/hour by liver)
 - CNS depression - ↓cerebral O₂ consumption, potent anticonvulsant
 - Respiratory depression: especially initially – may be apnoeic for short period
 - Circulatory effects - ↓cardiac outputs, ↓vasomotor depression → peripheral vasodilation → ↓BP
 - Poor analgesia and prolonged hangover
 - Dose: 4 mg/kg – less for elderly, more for robust male
 - Complications: acute intermittent porphyria and IgE mediated hypersensitivity
- Propofol:
 - White, oil in water emulsions, 20 ml ampoules, 1% solution = 10 mg/ml

- Structurally different to barbiturates
- Highly lipid soluble: so rapid onset – and short duration due to rapid distribution, metabolism ($T_{1/2} = 35 - 50$ minutes) and delayed return from poorly perfused tissues (e.g. fat)
- Smooth induction, rapid recovery
- Poor analgesic
- Apnoea for about 30 seconds common
- More ↓BP but less nausea/vomiting than thiopentone
- Induction dose: 2 mg/kg in young and 1.5 mg in elderly
- Midazolam:
 - H₂O soluble benzodiazepine
 - Muscle relaxant, amnesic, anxiolytic, anticonvulsant
 - Rapid onset and rapid elimination ($T_{1/2} = 2$ hours) cf. other benzodiazepines
 - Unlike other iv anaesthetics can be reversed, with flumazenil
 - Used for minor procedures, ICU sedation
 - Slower, more variable induction cf. thiopentone. Small dose may → deep anaesthesia
 - Dose for sedation: 1 – 5 mg titrated
 - Dose of induction: 10 – 15 mg (highly variable)
- Ketamine:
 - Related to angel dust
 - Dissociative anaesthesia
 - BP and respiration well supported, bronchodilator
 - Dose for induction: IV 1 – 2 mg/kg, IM 5 – 12 mg/kg
 - Smaller doses → potent analgesia
 - A sympathetic stimulant, can have bad dreams

Neuromuscular Blockade

- Muscle relaxants are used to:
 - Facilitate intubation and artificial ventilation
 - To facilitate abdominal access during abdominal surgery
 - To allow lighter levels of anaesthetic to be used → rapid recovery and less cardiovascular depression
- Block neuromuscular transmission from motor nerve to voluntary muscle (ACh transmission across synaptic cleft, broken down by cholinesterase)
- Non-depolarising blocking agents:
 - Competitive antagonists of the nicotinic cholinergic motor end plate receptors. E.g. rocuronium, pancuronium, atracurium, vecuronium
 - Degree of block determined by train of four stimuli. Each successive twitch is a lower amplitude – trails off. No interference with twitch response until 75 – 80% receptors blocked. 90 – 95% block required for surgery
 - Reversed by anticholinesterase drugs: neostigmine (onset in 2 minutes, lasts 20 minutes), pyridostigmine, edrophonium. Inhibit acetylcholinesterase → ↑ACh, but also effects muscarinic sites in parasympathetic nervous system. Side effects include salivation, bronchospasm, ↑gut motility and bradycardia. These effects blocked by atropine – which blocks the parasympathetic system
 - Analgesia ended with anticholinesterase (commonly neostigmine 2.5 mg) and atropine 1.2 mg
- Depolarising Neuromuscular Blocking Agents:
 - Faster onset and shorter duration (4 – 6 mins) than non-depolarising. Used for short procedures (quick intubation), supplemented with non-depolarising for long procedures or given by constant infusion
 - Suxamethonium: reacts with ACh receptors to produce depolarisation (→ fasciculation), but because it is not so rapidly eliminated as ACh, depolarisation persists → inexcitability of membrane around endplate. Repolarisation happens when suxamethonium is hydrolysed by pseudocholinesterase (unless atypical genetic variant → prolonged effect). If overdose or poor elimination → drug-receptor complex forms, unavailable for ACh → dual or phase II block. No antagonist to suxamethonium except fresh frozen plasma (contains pseudocholinesterase)
 - Train of four different to competitive antagonists: each twitch the same height (although reduced over normal)
 - Has other muscarinic side effects due to similarity to ACh: ↑BP, ↑intra-ocular pressure, ↑bronchial secretions, ↓heart rate, post operative muscle pain

- Suxamethonium is contraindicated in major burns, neurological injuries, hyperkalaemia, myasthenia and myotonic diseases, ↓pseudocholinesterase and history of malignant hyperthermia

Pain Management

- See also Symptom Management in Cancer, page 470

Pain Physiology

- Pain is vital to survival, but also an important source of human suffering
- Subjective response to:
 - Damage to body tissues → stimulation of somatic and visceral nociceptors (nociceptive pain)
 - Altered function of brain or nerve pathways: neuropathic pain
 - No detectable damage ⇒ psychological, social or environmental factors – idiopathic pain (diagnosis must include a psychological assessment)
- Three types of pain:
 - Acute pain: injury, surgery, acute illness
 - Cancer pain
 - Chronic non-cancer pain
- Nociceptive pain:
 - Nociceptors are free nerve endings stimulated by chemicals (e.g. H⁺), pressure or hot/cold
 - Sensitivity to noxious stimuli ↑ by prostaglandins (long chain fatty acids derived from arachidonic acid), e.g. PGE2 and PGF2
 - Conducted by
 - Fast, myelinated A fibres → sharp pain
 - Slow, poorly myelinated C fibres → dull persistent pain
 - Terminate in thalamus. Fast fibres then to sensory area of cortex → pain localisation. Slow fibres synapse with reticular formation → general arousal and → limbic system (autonomic responses and emotion)
- Facilitation:
 - Processes that ↑ pain sensation
 - Primary hyperalgesia: sensation heightened in discrete area due to histamine and serotonin sensitising adjacent nociceptors
 - Windup: hyperalgesia beyond areas actually damaged – due to recruitment of other receptors, mediated by NMDA
 - Cortical factors: facilitate pain in anxiety, stress, absence of other sensory input (e.g. at night)
 - Long term changes in pain pathways → pain disorders persisting after tissue damage has resolved
- Inhibition:
 - Descending fibres activate encephalinergic neurones within dorsal horn
 - Release encephalins which inhibit passage of pain impulses, derived from endorphins (in turn derived from β-lipoprotein). Can be antagonised by naloxone
 - Gate theory: large fibres send inhibitory collaterals to presynaptic C fibres
- Referred Pain: visceral pain felt in somatic structures.
- Adverse effects of pain:
 - Psychological effects - adaptive behaviour may become dysfunctional → stress, dependency, isolation, sleep deprivation, psychiatric illness
 - Neurohumoral reflexes - ↑ sympathetic activity, CVS system stimulated, metabolism becomes catabolic (which can inhibit healing), changes in immune system
 - Cardiorespiratory effects: e.g. decreased ventilation, ↓ secretion clearance → hypoxia (especially given ↑cardiac O₂ requirements), infection
 - Musculoskeletal spasm
 - Gastro and urinary function - ↑ secretions, ↑ sphincter tone, ↓ motility → stasis, urinary retention

Pain Pharmacology

- Opioid analgesics:
 - Main drugs used in severe pain
 - Act on Mu, kappa and delta receptors in substantia gelatinosa and solitary nuclei in spinal cord, thalamus, periaqueductal grey matter and amygdaloid
 - Different opioids have different affinities for different receptor subtypes → different effects. E.g. Morphine agonises all receptors giving strong analgesia, respiratory depression (both mediated

through M receptor) and dependence. Pentazocine is a weak M-receptor antagonist and strong k-receptor agonist and produces weaker analgesia, low dependence and little respiratory depression

- Uses of opioids:
 - Relief of pain
 - To supplement regional and general anaesthesia
 - As primary anaesthetic agents
 - Premedication to allay anxiety and sedate
 - Specific indications e.g. pulmonary oedema
- Alfentanil, fentanyl and remifentanil are opioids used intra-operatively because they are rapid and short acting
- Side effects: respiratory depression (if dose greater than that necessary for analgesia), addiction (not a problem in severe or post-operative pain), sedation, nausea and vomiting, constipation, cough suppression, histamine release
- Post-Operative pain relief:
 - Why:
 - Humanitarian reasons
 - Prevent stress and cardiac and endocrine responses
 - Improve ventilation (especially after abdominal surgery)
 - Hasten mobility → ↓ complications (e.g. DVT)
 - Reasons for poor pain relief: lack of understanding/recognition, poor knowledge of drugs and doses, fear of overdose or addiction, logistic difficulties (e.g. access to controlled drugs), willingness to complain about pain, lack of time, problems with side effects, variation in plasma levels necessary to produce analgesia, wide variations in pharmacokinetics
 - Factors affecting response:
 - Lean body mass
 - Age: neonates sensitive, elderly have slower distribution and metabolism
 - Liver disease → slower metabolism, renal disease → slower elimination
 - Problems in shock: smaller blood volume, but poorer diffusion. Give little and often and titrate to effect
 - ↓PaCO₂ → ↑plasma concentration
 - Drug interactions (e.g. phenytoin → ↓ pethidine clearance)
 - Personality type
 - Alternatives to IM opiates:
 - Continuous iv infusion: morphine 10 – 20 mg loading dose over 45 – 60 minutes followed by 2 – 3 mg/hour
 - PCA
 - Extradural or regional block
 - NSAIDs as adjuncts
 - TENS: transcutaneous electrical nerve stimulation, acupuncture and hypnosis
- Chronic Non-cancer Pain relief:
 - Opioids: orally (morphine tablets, methadone, codeine), epidural, subcutaneous
 - NSAIDs
 - Chemical or surgical ablation of nerves: e.g. chemical coeliac plexus block for pancreas pain
 - Psychological/emotional support
- Neuropathic pain (e.g. nerve compression, post herpetic neuralgia, etc):
 - Burning, stabbing, shooting pain
 - Treatment:
 - Amitriptyline: 10- 50 mg nocte, increases descending inhibitory pathways, effect in 48 hours
 - Anticonvulsants (Carbamazepine, Gabapentin)
 - Sympathetic blockade
 - Steroids to reduce inflammation of nerves or adjacent tumour
 - Plus TENS, psychotherapy, rehabilitation, opioids
- Bone Pain:
 - NSAIDs
 - If bony metastases: bisphosphonates

Local Anaesthesia

- Reversible inhibition of conduction in peripheral nerve fibres and nerve endings

- If local and general GA used, then local can take the place of an opioid in balanced anaesthetic
- Methods of local anaesthetic:
 - Surface or topical anaesthesia
 - Infiltration anaesthesia
 - Conduction anaesthesia or regional nerve block
 - Intravenous regional anaesthesia (into limb with a tourniquet)
 - Central neural blockade (e.g. spinal or epidural)

Local Anaesthetic Agents

- Reversible inhibition of conduction in nerve fibres and endings
- Classification:
 - Esters of benzoic acid: cocaine, tetracaine
 - Esters of para-aminobenzoic acid: chloroprocaine, procaine
 - Amides: e.g. lignocaine and bupivacaine (Marcain)
- Bind to internal opening of Na channel, preventing threshold and progression of action potential
- Pharmacokinetics depends on:
 - Mass movement of drug around and away from nerve
 - Diffusion into axon: best if unionised (i.e. weak base)
 - Absorption is determined by route of administration, site of administration (e.g. vascularity), and presence of vasoconstrictors (some anaesthetics themselves have vaso-constricting/dilating properties)
 - Metabolism: esters hydrolysed by plasma cholinesterase, amides by liver
- Adverse effects:
 - CNS: first cause excitation due to suppression of inhibitory neurons
 - CVS: negative inotropy, depression of conduction, reduction in automaticity (\rightarrow sinus bradycardia)
 - Vasoconstriction – decrease rate of absorption, \downarrow bleeding. Never use adrenaline in digital extremities \rightarrow ischaemia
 - Allergy: extremely rare
 - Fainting
- Treatment of overdose of local anaesthetic:
 - O₂
 - Diazepam/thiopentone for convulsions
 - Other resuscitation: airway, ventilation, elevate legs, IV fluids, atropine for bradycardia
- Clinical uses:
 - Topical anaesthesia: slow. Good for cannulating kids but takes an hour
 - Infiltration: e.g. around suturing. Don't inject through wound edge of unsterile wound
 - Nerve block: large area of analgesia, fewer injections, smaller doses
 - Extradural: between dura mater and periosteum of vertebral canal. Also blocks autonomic efferent nerves \rightarrow vasodilation \rightarrow hypotension. If it goes into subarachnoid space \rightarrow total spinal: respiratory paralysis, hypotension – treat with IPPV O₂, IV fluids and vasopressors
 - Spinal/subarachnoid anaesthesia: direct into CSF. More potent, more pronounced motor block
 - Intravenous regional anaesthesia: tourniquet inflated to 100mmHg above systolic blood pressure

Obstetric Anaesthesia

Physiology of Pregnancy

- Respiratory:
 - Raised diaphragm \rightarrow \downarrow functional residual volume
 - \uparrow O₂ demand: due to \uparrow maternal metabolism and foetal demands
 - \uparrow Respiration \rightarrow respiratory alkalosis (PCO₂ approx. 32) with metabolic compensation
 - \Rightarrow Becomes apnoeic more quickly
- Cardiovascular:
 - \uparrow Blood volume, \uparrow Hb by not so much \rightarrow physiological anaemia
 - Blood pressure: if normal pregnancy then small \downarrow in systolic, $\downarrow\downarrow$ in diastolic due to vasodilation
 - Minimum Alveolar Concentration (MAC) lowers in pregnancy
 - Volume of CSF reduces \rightarrow \downarrow dose of spinal by 2/3
- GI: lower oesophageal sphincter less effective \rightarrow \uparrow regurgitation

General Anaesthetic in Pregnancy

- More difficult getting endotracheal tube in: throat is smaller, usually done at night in emergency, etc
- Mendelsohn's syndrome: acid aspiration in surgery when pregnancy → bigger A-a gradient compared with non-pregnant. Give H2 blockers to ↓stomach acid
- ↑Awareness: inhaled and induction agents cross placenta – so often more cautious dosing. But muscle relaxants don't cross placenta. Usual dosing. But can't tell if they're aware
- So trend from GA to epidural in pregnancy
- If doing GA: use rapid sequence induction. Use anaesthetic agent, muscle relaxant and cricoid pressure to occlude oesophagus until tube in

Pathology in Pregnancy

- Pre-eclampsia: ↑BP, proteinuria, oedema
- Eclampsia: ↓ circulating blood volume, swollen tissues, fits, death
- Placenta praevia: placenta over os → big bleed
- Abruptio: placenta separates from uterus → big bleed
- Amniotic fluid embolism → equivalent of PE and DIC
- Aorta-caval occlusion/compression. → faint when they lie down. Uterus compresses IVC → ↓venous return → ↑HR and vasoconstriction → ↓perfusion pressure to uterus. Lie on left side, push uterus to left if doing CPR

Analgesic Drugs In Labour

- Mechanism of pain:
 - Ischaemic pain during contractions is due to ↓O₂
 - Contraction against resistance → colicky pain (like gallbladder)
 - Mechanical: pelvis and perineum
- Epidural:
 - Very effective
 - Good in eclampsia and where high suspicion of intervention
 - Complications:
 - ?↑ Rate of subsequent intervention
 - Hypotension
 - Paralysis, infection, haematoma, wrong drug
 - If into subarachnoid → total spinal overdose
 - If into vein → cardiotoxic drugs, CNS damage
 - If CNS drains out, positional headache
 - Can't have epidural if:
 - Patient refusal
 - Hypovolaemic due to haemorrhage
 - On anticoagulants, in case puncture epidural vein → haematoma
 - Septic: could transfer bug from blood to CSF
- Inhalational – N₂O/Nitrous Oxide: variable satisfaction, analgesia and dissociative, 50% vomit, 2 min to peak effect, no further effect once breathed out
- Opiates (e.g. Pethidine): variable satisfaction, dissociative, safe (midwives can use it), can → respiratory depression in neonate
- Psychoprophylaxis: very effective. If frightened and don't know what's going to happen, hurts more

Preoperative Assessment

- Aim is to investigate and optimise treatment for pre-existing medical conditions before surgery – especially respiratory and CVS
- ASA status = American Society of Anaesthetics: 1 = normal, 5 = expected to die, appended E = emergency
- Cardiovascular conditions requiring assessment:
 - Hypertension: 1/3 develop intraoperative hypotension, and 1/4 develop post-operative hypertension. Predisposes to MI, stroke and renal failure. Resting diastolic pressure over 100 mmHg should delay elective surgery until better controlled. Continue previous antihypertensive therapy up to and following surgery to prevent rebound hypertension (esp beta blockers)
 - Coronary vascular disease: IHD → 10-fold increase of risk of perioperative myocardial infarction. Delay elective GA until 3 (preferably 6) months after an MI

- Cardiac failure: contra-indication to all but most necessary surgical procedures
- Arrhythmias: resulting complications more related to underlying pathology rather than rhythm. If cardiac efficiency already reduced, GA can lead to ↓↓ cardiac output (e.g. atrial fibrillation with rapid ventricular response)
- Valvular and congenital heart disease. E.g. aortic stenosis may require anticoagulant therapy (although this increases haemorrhage risk so stop during operation) and prophylactic antibiotics
- Respiratory conditions requiring assessment:
 - Ventilation, gas exchange, cough and mucociliary clearance impaired by GA and into post operative period
 - Major risks: sputum retention, lung collapse, infection, ventilatory failure
 - Preoperative management aims to:
 - Eradicate infection
 - Reduce excess sputum production
 - Treat reversible obstructive disease
 - Treat co-existing right heart failure
 - Optimise ventilatory muscle function
 - Elective surgery should be cancelled if acute infections up to 5 weeks beforehand. (e.g. viral infections → ↓mucociliary clearance)
 - PEFR (Peak expiratory flow rate), FEV1 and VC (Vital capacity) are useful preoperative measures
- Endocrine:
 - Diabetics are at risk from:
 - Poor perioperative control: e.g. during pre-operative fasting, stress response, etc. Poor control → poor wound healing, ↑ infection, etc
 - Co-existing cerebral, coronary or renal vascular disease or autonomic neuropathy
 - Hyperthyroid patients at risk of CVS collapse
- Liver Disease: hepatic function commonly deteriorates post operatively. Infection risk to staff from hepatitis
- Alcoholism: complications include withdrawal, nutritional abnormalities, existing cardiac and liver disease
- Anaemia: increases risk of hypotension and hypoxia
- Drugs: Corticosteroids suppress cortisol, so patients will require supplementation with hydrocortisone at induction and by infusion following

Guidelines

- GP and RMO should:
 - Determine what medical conditions are present
 - Quantify any impairment and improve as much as possible
 - Make sure appropriate investigations are back in sufficient time before surgery
 - Advise patient of risks and benefits and obtain consent
- Conditions of note:
 - Cardiac: MI in previous 6 months, evidence of left or congestive heart failure, unstable or increasing angina, diastolic blood pressure > 110 mmHg, digitalis toxicity, uncontrolled AF
 - Respiratory: respiratory infections, exacerbation of CORD/Asthma
 - Hepatitis
 - Recent stroke
 - Thyroid or adrenal dysfunction
 - Poor control of diabetes
 - Major nutritional disorders
- Are the following present:
 - Family history of anaesthetic problems
 - Previous anaesthetic problems
 - Malignant hyperthermia (hypermetabolic response to gases or suxamethonium due to Ca leakage from cytoplasmic reticulum), suxamethonium apnoea, porphyria (thiopentone precipitates a crisis)
 - Abnormal hepatic or renal function
 - Muscle disease
 - Previous jaundice following anaesthesia
 - Allergy to anaesthetic or related drugs
 - Disorders of blood or coagulation

- On MAOIs or cholinesterase inhibitors
- Also investigate Hb, U+E, CXR, ECG and Respiratory function if indicated

Surgical and Fluid Management

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Normal Values

Blood volumes

- Infant 80-85 ml/kg
- Young child 80 ml/kg
- Adult 70 ml/kg

Child's body weight

- Under 9 years: kg = 2*age + 9
- 9 and over: kg = 3*age

Electrolyte concentrations

	Extracellular	Intracellular
Sodium	140	12
Potassium	4	155
Magnesium	1	28
Chloride	100	10
Bicarbonate	28	10
Phosphate	1	105

Fluid Compartments and Control

- Fluid Compartments in 70 Kg person:
 - Extracellular: 14 L
 - Intravascular: 3.5 L
 - Interstitial: 10.5 L
 - Intracellular: 28 L
- Female: 55% water, male 60 % water
- Control through ECF osmolarity:
 - Thirst
 - ADH: controls H₂O excretion
 - Renal Na excretion: renin-angiotensin-aldosterone system

Replacement fluids

Signs of extracellular fluid depletion

- Symptoms: oliguria (min 0.5 ml/kg/hr), thirst, tachycardia, dry tongue, weakness, confusion
- Signs: weight change, ↓tissue turgor, postural hypotension, cool peripheries, dry axilla and mucous membranes, ↓JVP
- Common in surgical patients due to: vomiting, ileus, stomal losses, etc. Not always naso-gastric losses. Frusemide is a flogging offence! It's due to intravascular hypovolaemia
- Investigations:
 - Bloods: ↑Hb, ↑Urea/Creatinine, Na/K
 - Urine Na
 - Maybe ABG for acid/base balance
- Replace deficit quickly over 30 minutes – 1 ½ hours, not by increasing hourly rate
- Give boluses of 200-250 mls N/saline, Hartmanns or plasma expander
- Take care in older patients/CHD: don't tolerate large Na loads (→ pulmonary oedema)
- If on IPPV, this pushes up intra-thoracic pressure to 10 – 15 cm H₂O (0 – 5 cm H₂O is normal), so when using central venous pressure need to adjust for this before determining whether hypovolaemic

Depletion in children

- Can be rapid and profound. Described as:
 - Mild: loss of 4 – 5 % body mass. History of diarrhoea/vomiting but few signs
 - Moderate: loss of 6 – 9 % body mass. Sunken eyes & fontanelle. Urine output < 0.5 mls/kg/hour
 - Severe: 10% loss of body mass. Very ill. Hypotension and rapid weak pulse
- See Management of Mild-Moderate Dehydration, page 650, for fluid management in children

Types of Replacement Fluids

- Crystalloids: isotonic, short intravascular $T\frac{1}{2}$. For replacement of extra-cellular loss. To replace blood give 3 times blood loss
 - 0.9 % saline: 154 mmol/L NaCl (isotonic)
 - Hartmanns and Lactated Ringers: electrolyte mixture similar to plasma
 - Excessive replacement of plasma losses acutely with saline may \rightarrow hyperchloraemic acidosis
- Dextrose containing solutions: not for replacing blood loss (hypertonic). For treatment of water loss or when sodium restrictions are present:
 - Barts: 4% dextrose/0.18% saline – 30 mmol/L NaCl + 168 Kcal/L
 - 5% dextrose: 200 Kcal/L (calories and water only)
- Synthetic Colloids: isotonic, long intravascular $T\frac{1}{2}$, for blood volume replacement. More readily available than blood and no infection risk, don't require cross matching. Give 1:1 ratio with blood lost. If > 1 L required, consider albumin and/or blood. Kidneys take time to excrete, so watch for fluid overload, especially in renal impairment and kids
 - Haemaccel: polygeline (degraded gelatine) plus electrolytes (145 mmol/L NaCl + 5.1 mmol/L K+ + 6.25 mmol/L Ca). $T\frac{1}{2} = 4$ hours, hypersensitivity rare
 - Dextran 40, 70: dextran with molecular weight 40K ($T\frac{1}{2} = 2 - 4$ hours) or 70K ($T\frac{1}{2} = 6$ hours), hypersensitivity reactions, impairs coagulation and cross match
 - Hetastarch (Hespan), Pentaspan: starch solution, MR = 70K, $T\frac{1}{2} = 17$ hours, hypersensitivity rare
- Blood products: reserved for > 20% blood loss or continuing bleeding or Hb acutely < 70 g/L
- If fluids not hypo-osmotic compared with blood, then red cell would swell \rightarrow haemolysis
- Warm fluids, especially if refrigerated. Haemaccel and crystalloids can be microwaved

Child Requirements

- Maintenance fluid: 4% dextrose + 0.18% saline + 20 mmol KCl/L at:

	Per hour	Per day
First 10 kg	4 mls/kg	100 mls/kg
Second 10 kgs	2 mls/kg	50 mls/kg
All subsequent kgs	1 ml/kg	25 mls/kg

- Losses (e.g. nasogastric tube, fever, diarrhoea) replaced with an equal volume of 0.45% NaCl + 20 mmol KCl/L. Give as boluses of 20 ml/kg over 15 – 30 mins. Losses decrease with renal failure
- See Management of Mild-Moderate Dehydration, page 650

Adult requirements

- Adult daily requirements:
 - 2.5 - 3 litres of fluid
 - 100 mmol Na (60 mmol/day in elderly)
 - 60 mmol of K+ (max of 10 mmol per hour)
- Can be given as:
 - 2.5 – 3 litres of dextrose/saline (=0.18% saline + 4% dextrose) per day with 20 mmol/L KCl in each bag, or
 - 2 litres of 5% dextrose and 500 mls of saline
 - Run in at 50 – 100 mls per hour (NB, smaller daily requirements for a small person)
 - If concerned about heart failure/pulmonary oedema than monitor saturation
- Intraoperative fluid replacement:
 - Oral intake withheld before surgery
 - In major surgery, half the estimated 24 hour maintenance requirement should be given initially (600 – 1000 ml saline), followed by maintenance requirements plus losses
 - K is usually excluded for first few post-operative days: due to \uparrow liberation from cells
 - Excess use of low Na fluids post-operatively may cause hyponatraemia given \uparrow ADH

Abdominal losses

- GIT has huge internal economy of fluid secretion & absorption
- Losses through surgical intervention (stoma, leaking viscous, etc) replaced with iv solution of similar composition

	mls Per day
Saliva	1500
Gastric	1500
Pancreatic	700
Biliary	500
Jejunostomy	2-3000
Ileostomy	500
Colostomy	300
Diarrhoea	0.5 – 15,000 (Normal ileum delivers 1200 – 1500 per day)

- See also Abdominal Physiology, page 154
- Diarrhoea and Vomiting
 - Leads to dehydration, hyponatraemia, hypokalaemia, hypochloraemia
 - Replace $\frac{1}{2}$ calculated losses in first 24 hours with saline plus potassium. Maximum rate of potassium replacement is 20 mmol/hr

Burns

- Burns → rapid loss → secondary organ damage (e.g. renal)
- Give 2-4 mls/kg * %burned area of Hartmanns: half over first 8 hours, rest over next 16, *in addition to* maintenance requirements. Consider blood transfusion
- See Burns, page 486

Monitoring adequacy of Fluid Replacement

- Monitor pulse, BP, respiratory rate and urine output (i.e. put in catheter):

	Per hour
Infants in Nappies	2 mls/kg
Kids & adults	1 mls/kg
Elderly	0.5 - 1 ml/kg

- Na to K ratio in urine should be > 1 . If < 1 then body frantically reabsorbing Na \Rightarrow not in balance

Postoperative Hyponatraemia

- See Hyponatraemia, page 107

Blood Products

Blood loss

Blood Loss	Clinical signs	Treatment
10% loss (500 ml)	↑HR, BP normal	Crystalloids, 10 – 20 ml/kg
20% loss (750 – 1500 ml)	↑HR, moderate hypotension	Colloid +/- red cells, 20 ml/kg
20 – 50% loss (1 – 2.5 L)	Severe hypotension, shock	Colloid and red cells 30 ml/kg
> 50% loss	?irreversible shock	Red cells + coag factors (FFP) and platelets

- Giving blood isn't based on how much they've lost, but on Hb measurement and pre-existing cardiac/respiratory disease. A normal person could survive an Hb of 50 if volume was adequate (below this CO falls dramatically). But a sick, old person can't use ↑CO to compensate, so CO starts to drop below 100

Blood Component Therapy

- Modern transfusion therapy is blood component therapy
- Blood components are used to:
 - Correct intravascular volume (usually non-human products e.g. crystalloids)
 - Correct O₂ transport deficiency
 - Correct bleeding disorders
- Blood components available:
 - Red cells: one unit is the red cells from one unit of donated blood (450 ml). Hb increases by 10 g/L per unit transfused. Red cell transfusions – transfuse at 1 unit per 2 – 4 hours (if

- cardiovascularly healthy then 2 hours, if older then 4 hours as you don't' want to go too fast otherwise volume overload)
- Platelet concentrates: Prophylactic platelet transfusions – 10 g/L pretty good maintenance level in leukaemia.
 - Fresh frozen plasma: 250 ml will provide approx 8% of an adult's circulating clotting factors
 - Cryoprecipitate: source of fibrinogen for DIC
 - VIII & IX concentrates
 - To separate these: centrifuge – take off plasma first, then platelets, then RBCs
 - Decision sequence:
 - What factor is deficient?
 - Is the deficiency physiologically significant (hard to decide. Not the same as below the normal range, as normal range includes functional reserve)
 - What is the appropriate blood product
 - What is the correct dose to transfuse
 - Has the transfusion worked?
 - When blood is required:
 - Type O immediately, type specific in 10 – 20 minutes and full X match in an hour
 - If massive transfusion (> 50% loss) use reconstituted red cells and colloid and consult haematologist re fresh frozen plasma (FFP), platelets and coagulation factors
 - Tests for coagulation during large transfusions should include:
 - Full blood count: baseline Hb and platelet counts before transfusion, and repeated throughout
 - APPT: intrinsic pathway
 - PT/INR: extrinsic pathway
 - Thrombin time: fibrinogen availability
 - Fibrin degradation products: for DIC
 - Risks:
 - Most common reaction to transfusion: febrile ½ an hour later:
 - Due to leukocytes contaminating red cells. If necessary, insert leucocyte filter on line (@\$50) → leucocyte poor red cells
 - Febrile reaction more common if multiple blood transfusions or multiple children (more antigenically primed)
 - ABO incompatibility (eg due to incorrect labelling):
 - Hypotensive, rash, tachycardia
 - Symptoms of major intravascular haemolysis: nausea, vomiting, low back pain (renal reaction to free haemoglobin), feeling very unwell
 - If allergic to plasma proteins → washed red cells
 - For immunocompromised: use irradiated red cells to stop leucocytes grafting into host & then attacking host
 - Infection risks (depend on prevalence in population):
 - Bacteria:
 - Yersinia Enterocolitica: is cryophilic (likes cold) and blood is a great culture medium. Comes from transient bacteraemia in infected donor.
 - Other bacteria: Brucella abortus, salmonella, M. Leprae
 - Viruses: HBV, HCV, HIV, HTLV-1, CMV, EBV
 - Parasites: Malaria, Toxoplasma gondii, Trypanosome cruzi
 - Specific risks:
 - HIV infection via transfusion: 1 in 1 – 2 million
 - CJD: no documented case worldwide (although has been done in animals)
 - HBV: 1 in 200,000
 - HBC: 1 in 80,000
 - Complications of massive blood transfusion:
 - Over transfusion → Fluid overload and pulmonary oedema
 - Coagulation defects: dilutional thrombocytopenia, ↓factors V, VII & X, DIC
 - Hypothermia (blood products are stored at 4 C)
 - Hyperkalaemia: K moves out of red cells in storage
 - Acidemia: stored blood becomes acidotic with age
 - Hypocalcaemia & citrate toxicity → cardiac depression and alkalosis
 - Hypomagnesaemia

- Transfusion haemosiderosis (ie iron overload) if on chronic transfusions (eg thalassaemia)
- Management of major reaction (either anaphylaxis/haemolysis or sepsis)
 - If worried during the transfusion, stop it
 - Call blood bank for advice
 - Send back blood + samples from the patient
 - Check for errors
- Strategies to stop transmission of infection:
 - Donor screening – very effective
 - Blood screening:
 - But tests not 100% accurate & window periods
 - Move from serologic tests to PCR for viral antigens

IV Cannulation

- Superficial veins of the arm: metacarpal, dorsal venous arch, cephalic (radial – thumb side), basilic (ulnar), median antebrachial, antecubital
- Parts of a cannula: bevel, stylet, catheter, hub of catheter, flash back chamber, air vent
- Cannulation procedure: blood return, level off, advance catheter, release tourniquet, pressure upstream remove stylet
- ↓Haematoma by ↓angle of insertion, ↓force
- Keeping it going: if infusion stopped, blood can track back through cannula and clot. Intermittent flushing with saline helps
- If hemiplegia, or mastectomy, insert in good arm
- Infiltration/tissuing is leakage into surrounding tissues. Will be pale, cold, boggy, painful. If red and warm then infection
- Phlebitis = inflammation of the vein. Caused by
 - Infection
 - Chemical irritation (eg antibiotics, especially erythromycin)
 - Mechanical
- Consequences of infection: inflammation of skin, cellulites or bacteraemia
- Minimising infection: hand washing, sterile equipment, site care and regular inspection
- Always record in notes: date and time of insertion, what gauge, what vein
- Replace every 72 hours, unless inserted in emergency in which case replace in 6 – 8 hours
- Consent: check armband, explain reasons for iv therapy, duration, what's being infused, possible complications. Obtain verbal consent
- Choice of gauge: age, flow required, what's being infused.

Gauge	Colour	Uses
24	Yellow	Neonates, extremely small veins
22	Blue	Infants, elderly, fragile veins, small lengths
20	Pink	Most commonly used
18	Green	For viscous fluids (eg blood)
16	Grey	For large quantities of IV fluid. Painful at insertion.
14	Orange	As for 16

Nutrition in Surgical Patients

Consequences of malnutrition

- ↑Perioperative mortality (e.g. in 30 days post surgery)
- ↓Healing
- ↑Respiratory infection
- ↓Immune function
- ↑Wound infection

Nutritional assessment

- Observe: thin?, how strong is finger grip
- History: intake over preceding days compared to normal
- Anthropomorphic measurement (BMI, girth to hip ratio, skinfold thickness, compare actual to standardised 24 hour urine creatinine excretion.)
- Lab measurements (albumin, transferrin – only for gross malnutrition)

- Physiological assessment (PEFR, FEV1, hand grip)

Energy Metabolism

- Adult needs 25 – 30 kcal/kg/day
- Typical diet gives: CHO – 40 – 60% (4 kcal/g)
Fat: 20 – 45% (9 kcal/g)
Protein: 10 – 20 % (4 kcal/g)
- Excess CHO stored as fat, otherwise broken down to glucose
- Short & medium chain FFA are directly absorbed into the portal vein: so if gut is malabsorbing, give them this – rapid and easy to absorb
- During starvation, FFA saturate Kreb's cycle → ketones and acids

Protein Metabolism

- No body storage. Used, converted to energy or excreted
- Maintained by protein intake of 0.8 – 1.0 g/kg/day
- Nitrogen balance ⇒ nitrogen in equal nitrogen out
- Protein is 16% N₂

Energy metabolism in Starvation

- Immediate use: liver and muscle glycogen
- Early starvation: Gluconeogenesis from AA, glycerol and lactate. Leads to catabolism. Only supports CNS and RBCs
- After few days: ↓metabolism, ↑FFA used by heart, kidneys and muscles
- Prolonged starvation: brain uses ketones. Protein catabolism ↑ as fat stores used up

Nutritional Requirements

- Basal Energy Requirement (BEE) for otherwise well and sedentary (↑ when challenged by illness):
 - Men = $66 + (13.7 * \text{kg}) + (5 * \text{height in cm}) - (6.8 * \text{years})$
 - Women = $655 + (9.6 * \text{kg}) + (1.8 * \text{height in cm}) - (4.7 * \text{age})$

Nutritional Support

- Protein/Calorie Requirements
- Well nourished patients without sepsis or injury: H₂O and electrolytes OK for 5 days
- Non-depleted post-operative patients: **1.2 - 1.5 * BEE** + 0.8 – 1.0 g protein/kg/day to prevent catabolism
- Malnourished patients without sepsis or injury: Cautious repletion – avoid refeeding syndrome due to depletion of co-factors → marked ↓ in PO₄ and Mg – monitor
- Nutritionally depleted patients: 1.5 – 1.8 g protein/kg/day + 1.5 * BEE
- Patients with sepsis or injury: Well nourished can manage without feeding for a few days. Malnourished need feeding

Enteral Nutrition

- Adult energy requirements: 40 Kcal/kg/day (approx. 2,500 Kcal per day)
- Requirement ↑ in sepsis, burns, trauma by 50 – 100 %
- Protein requirement: 1.5g/kg/day (approx. 105 g protein or 14g N₂ per day)
- Enteral much safer and less expensive compared with parenteral
- Delivered by: NG tube, nasoduodenal tube (↓risk of aspiration), PEG, jejunostomy
- Problems: aspiration, tube blockage, diarrhoea due to intolerance/inadequate digestion
- Feed by pump, starting slowly, at 30 – 45 degrees. Stop at night if they can tolerate increased flow during day
- Tradeoffs:
 - When sick, ↓ motility and ↓emptying. Need to be minimal volume but still flow through tube
 - Don't include lactose as ↓lactase when sick. Lactose would → diarrhoea
 - ↑Osmolar load → ↑diarrhoea. So need ↑Mr
- 3 types:
 - Intact nutrient formulas: Blenderised feedings (don't flow well), lactose-free feedings (via tube), and nutrient-dense feedings (flavoured for oral use)
 - Pre-digested Nutrients (elemental diets): taste foul, use NG tube
 - Feeding modules: concentrated sources of one nutrient (e.g. protein, CHO or fat)

Parenteral Feeding

- For nutritional support when GI tract can't be used
- Via central line: Total Parenteral Feeding (TPN) has very high osmolality. X-ray after insertion to check no pneumothorax and line is outside pericardium (above anterior third rib) to avoid cardiac tamponade following catheter erosion
- Complete nutrition: electrolytes, glucose, amino acids, fat emulsion, vitamins, etc. Fat a good way of giving calories without ↑glucose (which could → diabetes)
- Other major risk: sepsis. Test for coagulase +ive staphylococci. Colony count should be 5 times higher in central line sample than in peripheral blood
- Metabolic problems common, e.g. hyper or hypo glycaemia, acidosis, etc. Alter constitution of TNP

Post-Operative Care

- Eg following a laparotomy
- Know and watch for complications
- Analgesia:
 - Epidural: watch for low blood pressure
 - PCA/PRN narcotic (but watch for constipation from morphine/codeine)
- Wound care:
 - Check not too much blood from drain
 - Rough times to leave a drain in for:
 - Laproscopic cholecystectomy/vascular surgery: 1 day
 - Rectal surgery: 3 –4 days
 - Mastectomy: 4 – 7 days (can go home with it in)
 - T-tube for biliary surgery: if latex then 10 – 14 days, if silicon then 3 – 4 weeks
- Anti-coagulant (eg Clexane)
- Fluid balance: if elderly alternate normal saline and dextrose bags (+KCl)
- NG tube:
 - If no aspirate after 24 hours then take it out
 - If aspirate is green, leave it in
- Prophylactic antibiotics: for uncomplicated laparotomy usually one dose intraoperatively
- Consider rehabilitation, support at home, work re-entry
- Plan follow-up

Post-Operative Complications

Infection

- Usually takes 3 – 5 days
- Wound infection:
 - Redness, induration
 - Either:
 - Abscess: red, hard mass → needs drainage
 - Cellulitis: red, hot, painful → antibiotics
- Abdominal infection:
 - Often 5 – 7 days before apparent: pain, ileus, sweats, rigours
 - Investigations (to look for abscess): Maybe US. CT better
 - Treatment:
 - Small abscess: if deep and < 3 cm try antibiotics
 - Large abscess: if > 4 cm then drain either surgically or under radiological guidance. Depends on depth, if its loculated or presence of overlying bowel
- Peripheral line
- Central line: may look innocent – but consider if no other locus found. Can leave a central line in for 4 – 6 weeks if you look after it
- Chest infection:
 - Usually results from atelectasis following poor ventilation (especially immediately following extubation, especially if pain)
 - Look for ↓saturation and fever (especially if it occurs the night following surgery) – this is initially due to inflammation – so it presents quicker than the above infections

- Management:
 - Effective analgesia
 - Chest physio: deep breaths and cough each hour
- Overall management:
 - Check wound, chest, iv sites, abdomen, UTI. Check for signs of meningism, endocarditis, DVT
 - Do FBC, culture. Consider MSU, CXR, abdo US

Decreased Blood Pressure

- Lie flat and give O₂
- Check pulse and other vitals
- Consider:
 - Hypovolaemia: check fluid chart, replace losses
 - Haemorrhage: review wounds
 - Cardiogenic: any heart history?
 - Sepsis
 - Anaphylaxis

Nausea/Vomiting

- Causes: Mechanical obstruction, paralytic ileus, emetic drugs (opiates, digoxin, anaesthetics), systemic or GI illness
- Consider AXR, NGT, antiemetic (metoclopramide or cyclizine)

Deep Vein Thrombosis

- If it's a long operation, a clot may start to form then and propagate → inflammation → mild fever
- If immobile or in pain, then may form post-operatively
- High probability of a DVT if:
 - Calf circumference > 3 cm than the other
 - Malignancy
 - Immobile
 - Local tenderness
 - Family history
- Test using Doppler US (for flow)
- See also Deep Vein Thrombosis (DVT), page 74

Confused Patient

- Ie Delirium. See also Delirium, page 442
- Causes (especially if already borderline):
 - Infection
 - Hypoxia
 - Metabolic: glucose, K
 - CVA or MI
 - Drugs:
 - Too little: eg withdrawal of sleeping pills, insufficient analgesia
 - Too much: eg morphine → ↓respiration, pinpoint pupils. Treat with naloxone (but short T½ so may need to repeat)
 - Delirium tremens (alcohol withdrawal)
 - Urinary retention
 - No cause found
- Management: Quiet, gently lit area, familiar faces. Consider midazolam or haloperidol

Decreased Urine Output

- = < 30 ml/hour
- Causes:
 - Hypovolaemia: ↑HR, ↓BP, peripherally shut down
 - Urinary retention: ?palpable bladder
 - Catheter blockage (especially if sudden drop off)
 - Renal failure due to hypotension, nephrotoxic drugs, transfusion
- Management: If not overloaded then treat with fluids: normal saline unless significant blood loss. Don't use dextrose – won't stay in the blood for long

Dehiscence

- = Wound breakdown (eg of a gut anastomosis). Usually after 5 – 7 days due to ischaemic tension, infection, etc
- Symptoms: severe pain, ↓bowel sounds
- Investigation: CT with gastrographin contrast

- Paediatric topics elsewhere:

- Skin conditions, including infections, eczema and other lesions, see Skin, page 313
- Consent and Children, see Consent, page 717
- Other cross references are included in the relevant section

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Epidemiology and Health Systems

Epidemiology

Measures of Child Health

- Measures of death/disease:
 - Mortality
 - Disease specific mortality/morbidity (eg SIDS)
 - Hospital Discharges
 - Disparities: ethic, gender, age, location, etc
- Measure of health interventions:
 - Immunisation coverage
 - Well child checks
- Measures of health or its determinants or impacts:
 - Breast feeding at 3 months, 6 months
 - Participation: early childhood education, school, sport, etc
 - BMI: marker of appropriate nutrition
 - Self-report (eg questionnaires)

NZ Statistics

- Numbers of children:
 - 23% of NZers are aged 0 - 14
 - Maori and PI children are about double adult proportions as percentage of total population – 1/3 of Maori and PI people are under 15, compared with 19% of Europeans
 - Until 2050, fall in the number of children, and fast fall in their proportion of the total population (from 23 → 16%) → future conflict over resources: “principle of first call” – essential needs of children should be given high priority in the allocation of resources
- Socio-economic status:
 - Children with no parent participating in the labour force (1996): European 13%, Maori 42%, PI 37%, Asian 30%
 - Proportion of children in one-parent families (1996): European 15%, Maori 43%, PI 27%, Asian 12%. Increased over all groups from 1986 to 1996
 - Maori and Pacific Islanders also more likely to not have a car, share a household, less likely to leave school with a qualification
- Mortality:
 - Under 5 mortality currently around 500 per annum
 - Age specific rates: 7/1000 live births for 0 – 1 years, 0.4/1000 for children 1 – 4 years, 0.2/1000 after this
 - All child mortality rates in NZ have declined by 1/3 over the last 15 years, but this is slow in comparison with other countries. Our OECD ranking for under 5 mortality has fallen from 6th to 15th. If we had had the same fall as Sweden 194 children would not have died.
 - Major causes of death:
 - < 1 year: SIDS (29%), Congenital abnormalities (28%), Perinatal conditions (27% - prematurity, neonatal infection, hypoxia, etc)
 - 1 – 4 years: Injury and poisoning (46%), Congenital abnormalities (18%), Cancer (11%). Maori injury and poisoning rate 3.5 times Non-Maori
 - SIDS rate has fallen from 4/1000 in 1989 to 1.5/1000 (UK is 0.6/1000). Rate 4 times higher in Maori than non-Maori. Low income 3 times higher income (independent of ethnicity) – due to risk factors of maternal smoking, teen pregnancy, single parenthood, etc
- Morbidity:
 - Under 1's most likely to be admitted: NICU, respiratory GI and infectious
 - Ethnicity patterns same as for mortality: Maori rates range from 1.7 – 4.6 times higher
- Conclusions:
 - Despite improvements, New Zealand hasn't made the gains that other countries have
 - Ethnic and socio-economic disparities are growing
 - Improvements in curative medicine are unlikely to have an impact on this inequality

Health Systems

- Determinants of child health:
 - Biology: genetic, development in utero
 - Socio-economic:
 - Housing
 - Income
 - Education (especially maternal – key issue in 3rd world)
 - Environment:
 - Social
 - Physical
 - Health Behaviours
 - Health Services
- Impact of determinants:
 - Perinatal complications and family adversity have an *independent* impact on cognitive ability
 - Social adversity is a bigger factor in mild mental retardation than biological factors
 - Variations in family social background is a:
 - Weak determinant of specific problems
 - Pervasive determinant on generalised vulnerability to a wide range of problems
 - Large differences in absolute income have little or no effect on mortality. Small increases in income equality have a large effect
- Improving health equality through health services:
 - Population based measures:
 - Resource allocation
 - Intersectorial collaboration
 - Community development
 - Data collection on deprivation
 - Salaried GP services for deprived areas
 - Individual health services:
 - Site and mode of provision of services
 - ↑Communication with consumers
 - Targeting of preventative services

International Agreements

- Alma Ata Declaration on Primary health Care:
 - Declaration to protect and promote the health of all people
 - ‘Health for all by the year 2000’ through quality primary care
 - Defined primary care and gave principles for health services
- Ottawa Charter on Health Promotion: [See Health Promotion, page 691]
 - Building health public policy
 - Creating healthy environments
 - Strengthening community action – power and control to communities to identify and solve their problems
 - Helping people to develop their own skills
 - Reorientating the health system: balance between preventative and curative services
- Jakarta Declaration on Health Promotion in the 21st Century:
 - Comprehensive approaches (using all 5 Ottawa charter principles) are the most effective
 - Settings offer practical opportunities for the implementation of comprehensive strategies
 - Participation by the community is essential
 - Health learning fosters participation
- United Nations Convention on the Rights of the Child:
 - Principles and standards by which governments, organisations and families can be measured
 - Ratified by NZ in 1993
 - Rights:
 - Article 18.2: “render appropriate assistance to parents and legal guardians in the performance of their child-rearing responsibilities
 - Article 23: Rights of mentally or physically disabled children: “full and decent life.... Dignity ... self-reliance Active participation in the community”

- Article 24: Right of all children to “the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health”
- Most recent assessment of NZ raised concerns about:
 - Fragmented approach to the rights of the child
 - Insufficient data collection on the effects on children of economic reform
 - “Extensive delegation of support services to children and their families” – but quality remains the responsibility of the state
- NZ Child Health Strategy 1999 had 6 future directions:
 - A greater focus on promotion, prevention and early intervention
 - Better co-ordination
 - Development of a national child health information strategy
 - Child health workforce development
 - Improve child health research and evaluation
 - Leadership in child health

History and Examination

Difference Between Adult and Child History Taking

- Kids may not be able to tell you, teens may not want to
- Concerned with nutrition: what normal and current feeding practices are, micro-nutrients
- Growth: weight, height and head circumference
- Developmental perspective:
 - Gross motor: rolling, sitting, crawling, walking, running, stairs, sports
 - Fine motor: hand skills, co-ordination (assessed through play → art → writing)
 - Vision
 - Speech/language and hearing
 - Social development: bonding → parents vs strangers → peers
- Immunisation: ‘Are your immunisations up to date’ – usually meaningless. Need to be more specific
- Family history:
 - Congenital abnormalities
 - Genetic factors
 - Parental age and experience
 - Impact of chronic illness on family
- Social history:
 - Abuse and neglect
 - Living circumstances – overcrowding, smoke exposure
 - Education settings, eg day care
 - Peer support for kids (eg in adolescence)
 - Adolescence: HEADSS Assessment (see page 666)

History Outline

- General data: name, DOB, Ethnicity, where they live
- Presenting Complaint
- History of presenting complaint:
 - Chronological and including symptoms across all systems
 - Treatments so far
 - Contact history
 - Family history of the complaint
- Paediatric Past Medical History:
 - Antenatal
 - Birth/perinatal: Gestation, delivery, weight, APGARS, any special care, complications
 - Feeding (breast, formula, solids) – detailed if relevant (eg which formula, how much, which solids, how much)
 - Weight – growth history, where relevant growth and puberty in family members
 - Immunisations
 - Milestones – including relevant milestones for the child now: Cover Gross and Fine motor, receptive and expressive language, social, play and self care skills. See Development Chart: normal development from 0-60 months, page 576

- Past medical history
- Social/school
- Medications
- Allergies
- Family History: ages and health of parents and grandparents. Ages, names and health of siblings
- Social History:
 - Parent's occupations
 - Who cares for the child
 - Schooling/childcare, performance at school
 - Behaviour at home/school
 - Sleeping arrangements and home circumstances
 - Financial circumstances
 - Alcohol, smoking
 - Pets
 - Problems/stresses at home
- Systems enquiry (OHCS, p 173):

	Neonate	Toddler	Older Child
Cardiorespiratory	Tachypnoea, grunts, wheeze, cyanosis	Cough, exertional dyspnoea	Cough, wheeze, sputum, chest pain
Gastrointestinal	D&V, jaundice, stool frequency	D&V, stool frequency	D&V, abdominal pain, stool frequency
Genitourinary	Wet nappies (how often?)	Wet nappies (how often?)	Haematuria, dysuria, sexual development
Neuromuscular	Fits, odd attacks, jitters, feeding ability	Fits, drowsiness, hyperactive, vision, hearing, gait	Headaches, fits, odd sensations, drowsiness, academic ability, vision, hearing, co-ordination
ENT and teeth	Noisy breathing	Ear discharge, teeth eruption	Earache/discharge, sore throat

- General questions: fatigue, lumps, itch, fevers, bleeding tendency, family interaction

Examination

- Principles:
 - Leave nasty things till last
 - Observe
 - Get on floor and use games
 - Wait until child familiar with environment but start before bored
 - Don't touch child until rapport established
 - Use your own toys – they're novel
 - Get parents to undress them (or do anything else that is nasty)
 - Get them to draw pictures while taking the history
- They're likely to be scared (depending on previous experience). Build rapport, play games, talk with child not through parent. Don't wear stethoscope around neck
- Show them what you want rather than telling them
- Blood pressure:
 - Is important – **always do it**
 - Getting them calm is hard – usually anxious → artefacts common
 - Cuff: Bladder should nearly encircle the arm. Width is 2/3 length from shoulder to elbow
- Chest exam:
 - Percussion more sensitive than auscultation (won't show anything in the absence of respiratory signs/symptoms)
 - Percussion will tell you about hyperinflation, fluid, mediastinal shift
 - Auscultate heart early in the exam – but not first
- Abdominal exam: Get child to suck in and push out tummy to check for tenderness – then you won't have to hurt them yourself.
- Differences in a baby:
 - More liver in the abdomen (2 finger breaths is normal). Don't press too hard – moves with respiration

- Pelvic organs higher (eg bladder)
- Pulses: Radial/ Brachial – take both sides. Must palpate femoral pulse. If feet aren't white don't take peripheral pulses
- Teenage girls: examine chest underneath clothes

Normal Values

Age	Breathing	Pulse	Systolic BP
< 1 yr	30 – 40	110 – 160	70 – 90
2 – 5 yr	20 – 30	95 – 140	80 – 100
5 – 12 yr	15 – 20	80 – 120	90 – 110
> 12 yr	12 - 16	60 - 100	100 - 120

- Stethoscope around your neck adds 10!
- Haemoglobin: at birth: 170, day 5: 200, 12 weeks: 120 (lower limit of normal is 90 – 100)

Examination outline

- Height, Weight and Head Circumference (and plot them)
- General:
 - Sick or well
 - Dysmorphic features
 - Obvious distress
 - Temperature
 - Colour/rashes/anaemia/cyanosis/jaundice
 - Lymph nodes: Check anterior and posterior cervical chains, subhyoid, sub-occipital, sub-mandibular, sub-lingual, axillary, inguinal and epitrochlear
 - Hydration/perfusion
- Cardiovascular:
 - Pulses: radial, femoral, synchrony, sinus arrhythmia (normal in all children)
 - Blood pressure (NB use correct cuff size)
 - JVP: often hard to see
 - Peripheral oedema (Periorbital in babies)
 - Liver enlargement → right ventricular failure
 - Feel the cardiac impulse: Apex may be more lateral in children. Thrills
 - Auscultation
- Respiratory:
 - Ears, throat, nose, sinuses
 - Clubbing
 - Chest deformity
 - Respiratory rate, effort and accessory muscle use, grunting, ability to talk in sentences
 - Intercostal, sub-sternal and supraclavicular indrawing, hyperinflation, Harrison's sulcus (lower ribs pulled in → chronic airways disease), pigeon chest (⇒ chronic ↑ in AP diameter), tracheal tug, nasal flaring
 - Auscultation, including cardiac dullness (⇒ hyperinflation). Tracheal position rarely of value
- Abdominal:
 - Inspection, movements, scars, hernia
 - Liver, spleen and kidneys
 - Bladder
 - Masses
 - Tenderness
 - External genitalia
 - Examine anus (PR rarely required)
- Neurological:
 - Developmental assessment: See Child Development, page 574
 - Neurological Exam: See Neurological Exam in Children, page 621
- Joints
- Skin

When is a child really sick?

- Factors which are **not** on their own discriminating between mild and severe:
 - Temperature: spikes easily

- Pulse: variable, eg ↑↑ if crying
- Blood pressure: hard to measure, and if shocked is still maintained till very late. As soon as they have *any* hypotension they're the same as an adult with no recordable BP
- Factors from **history** which discriminate:
 - Intake:
 - Refusal to feed ⇒ more severe
 - Refusal to take solids but still taking liquids ⇒ not so bad
 - Losses:
 - Vomiting:
 - Frequency and amount: if vomiting their whole feed then bad (vs a small spill)
 - Colour: Bile is bad. Yellow (from gallbladder), green (after bile has been in the stomach) or orange. Due to obstruction or ↑↑ sympathetic discharge, eg due to pain (not necessarily abdominal – could be a tormented testicle)
 - Decreased urine output (wet nappies < 4 per day)
 - Diarrhoeal losses
- Dysuria and pale extremities may be the only warning signs before they crash
- Factors which discriminate on **exam**:
 - Floppiness: ↓ tone
 - Perfusion: pale, mottled or blue, cold. **Capillary refill > 2 secs.** (ie Peripheral vasoconstriction)
 - Fitting
 - Cyanosis
 - Tachycardia
 - Respiratory rate: quality as important as rate
 - Rash if petechial/purpuric (?meningococcal septicaemia)
 - ↓ pH
 - ↓ Weight (dehydration)
- Toxic Appearance =
 - Decreased level of arousal
 - Circulatory compromise: pallor, tachycardia, cool + mottled limbs, hypotension
 - Respiratory impairment:
 - Tachypnoea, grunting respirations, recession, cyanosis
 - Due to ↑ O₂ requirements + trying to blow off CO₂ from acidosis + pulmonary oedema from capillary leak
- Shock =
 - Clinical diagnosis of failure of the circulatory system to deliver sufficient O₂
 - Look for compensatory mechanisms which try to maintain perfusion of vital organs (↑HR, peripheral vasoconstriction)
 - Causes of shock:
 - Capillary leak → ↓ cardiac output
 - Changed vascular tone
 - Impaired myocardial function
- Progression: Toxic → Septic → Shock
- Specific signs:
 - Meningism: bulging fontanel, rash, stiff neck
 - Pneumonia: chest sounds (not very sensitive)
 - Distended abdomen and guarding: obstruction, appendicitis
 - Lumps in the inguinal region (seen or felt): hernia → obstruction → acidotic
 - Blood in faeces: Intussusception
- Basic investigations:
 - Bloods: FBC, electrolytes, culture, ABG, (cross match)
 - X-rays: chest, abdomen if distended
 - Urine culture (bladder stab)
 - Maybe lumbar puncture

Neonates

- Check list for a neonate (clinical acumen less reliable):
 - Fever: consider full sepsis evaluation for any child > 38 C
 - Feeding: if intake < 50% normal

- Urine output: < 4 wet nappies in 24 hours
- Peripheral circulation: pallor of recent onset, mottling, cold periphery, slow capillary return
- Responsiveness: poor response to stimulation and a weak cry
- Activity: ↓movement, ↑sleepiness
- Breathing difficulty: signs of distress, cyanosis, RR > 60
- Apnoea: pause in respiration > 20 secs. Central (eg premature) or obstructive (eg URTI) or mixed
- Vomiting: treat any vomiting in neonate seriously. Look for bile staining
- Cyanosis
- Seizures
- Severe jaundice: risk of bilirubin encephalopathy

Dealing with Children and Families

Talking with Children

- Do:
 - Engage them
 - Explain who you are and why you are seeing them
 - Use language and concepts that are age appropriate
 - Reassure if seeing separate from parents
 - Outline confidentiality issues with older children or adolescents
- Don't threaten:
 - The child's sense of loyalty to their family
 - Their defences against unbearable emotional pain
- Interviewing preschoolers (3 – 5 years):
 - Get down to their level, use simple language
 - Take things at their pace
 - Can use play, drawings and stories
 - Ask about everyday world
 - Watch verbal and non-verbal communication
 - See with parent
- School age children (6 - 11 years):
 - Can be structured
 - Ask about feelings (sadness, anger, etc) as well as daily life
 - Ask about family, school, friends, problems, worries
 - Wishes, hopes for the future
 - Very abstract, open-ended questions can be confusing
- For adolescents see Talking with Adolescents, page 665

Parent and Adolescent Education

- Aim is to change behaviour. Changing behaviour requires:
 - **Knowledge:** necessary but not sufficient
 - **Skills:** to manage the change
 - **Motivation:** Involves striving towards a goal, not just 'trying'. The goal must be:
 - Important to the person – 'I want this'. Make it attractive. May need their goals to come before yours.
 - Achievable – 'I can do this'. Believe in them
 - Not too unpleasant. 'I don't mind doing this'. Make it easy
- Good counselling technique:
 - Open-ended questions: "tell me about..."
 - Active listening: "Hmm, I see..."
 - Reflection: reflect facts **and** emotions
 - Summarising: "Let me see if I've got this straight..."
 - *Don't* ask leading questions: eg "You don't do that, do you?"
- Take a history using open-ended questions, reflecting, summarising:
 - Help parent or adolescent clarify exactly what it is they want to know
 - **Knowledge:** what do you understand about...? Where did you find that out? How convinced are you?
 - **Attitudes/fears:** are you worried about anything in particular?

- **Practices:** What have you actually done so far?
- **Barriers:** What's stopping you from doing this?
- Then:
 - **Validate/reinforce** knowledge they already have: "That's terrific – you already understand a lot...."
 - **Education** to correct incorrect beliefs/address fears
 - **Encourage** them to find their **own solutions**: "So, what do you think you could do?"
 - **Reinforce** safe practices and responses
- See also Neonatal and Infant Anticipatory Guidance (Parent Education), page 590

Families

- Ref: notes from Lorraine Christie, Clinical Psychologist

Unuhia te rito o te harakeke
 Kei whea te komako?
 E hua whakatairantitia
 Rere ki uta, rere ki tai
 Mau e ki mai He aka te mea nui o te ao?
 Maki e ki atu, He tangata, he tangata

If you pluck the young shoot of the flax bush, where will you find the bellbird?

It will be fluttering about flying to the beach and sea!

What is the greatest thing in the world? I tell you, it is people, it is people

- The task of childhood is development:
 - Social relationships
 - Emotional maturity
 - Sound set of values and beliefs
 - Sound thinking patterns
 - Knowledge
 - Of body and skills
- Self esteem and self respect laid down in the first 7 years are influenced by: Gender, race, culture, sexuality, temperament, ordinal position, IQ, physical characteristics, creativity, did you arrive in the family at an okay time
- Families are systems with:
 - Structure
 - Various roles
 - Authority
 - Channels of communication
- Five characteristics of healthy families:
 - The marital relationship is the strongest relationship and the greatest focus of power
 - Communication is open and honest and permits spontaneous interruption
 - Warmth and caring predominates over anger and hostility
 - There are known problem solving techniques which can be instigated quickly
 - Movement towards independence for all members of the family
- The family life cycle: constant reorganisation and change
 - Two form a couple:
 - Take on husband/wife/partner roles
 - Substantial reorganisation of boundaries: family, friends, togetherness vs autonomy
 - Work through differences
 - Structuring a relationship: complimentary vs symmetrical
 - First baby:
 - Parenting roles
 - Ensure spouse relationship remains the strongest
 - Reorganised boundaries to allow for grandparents, friends, interests
 - Preschoolers:
 - Protect spouse relationship: contact, support, being together
 - Parent/child subsystem: affection, encouragement of appropriate autonomy, boundaries for child, individuating siblings from each other

- Continued reorganising of boundaries: grandparents, outside world, work
- School age children:
 - Integrating school and family systems
 - Allowing age appropriate autonomy
 - Children less egocentric, more sensitive to other's needs, develop sense of fairness and gender awareness
- Adolescence:
 - Issues of proximity and distance
 - Extending boundaries to allow independence
 - Continual renegotiation – autonomy vs control
 - Sibling individuation from each other
- Young Adult: between families
 - Differentiating self from family of origin
 - Leaving home, career development
 - Intimate peer relationships, courtship
 - Parents: at height of careers, retirement looming
 - Grandparents: needy, mobility, loss of sight, death
 - Parents take on grandparent roles

Preparing a child for surgery

- Talk to the child about what is going to happen and why. Read books about hospital
- Reassure your child that you will be there too
- Answer your child' questions
- Use simple terms that the child can understand
- Take a favourite toy. It can have bandages too
- Be honest without scaring: ‘It will hurt for a bit – but we’ll try and make it better’
- Tell the child he/she will be going home with you when it’s finished
- Don’t be surprised if the child gets angry with you: this is normal

The Dying Child

- Anticipated: preterm infants, congenital abnormalities, metabolic disease, etc
- Unanticipated: often older, trauma, SIDS
- Issues:
 - Relief of child’s pain → pain management, including neonates
 - Clear and simple information: check their understanding, explain prognosis, explain disease process, avoid information overload or jargon, respect silence
 - Decisions about when to withdraw treatment
 - Before death: time and space, preparation of child
 - After death: viewing the body, coroner, funeral options, surviving siblings, other families, availability of health care team
- See also Children’s Grief, page 459

Autopsy of a Child

- Family concerns:
 - What is an autopsy – like a major operation
 - Will my child be cut – yes
 - When will it be done – soon
 - How long will it take – max 3 hours
 - What will my baby look like afterwards – won’t see chest incision if dressed. Vertical cut down back of head
 - Can I take my baby home afterwards – yes
- Autopsy may provide:
 - A cause of death – but may take time
 - Identify unacceptable iatrogenic lesions
 - Quality control for a neonatal unit
 - Assist medical knowledge
 - Information that may help other babies

- Common reasons for refusal:
 - Concerns about disfigurement and further suffering
 - Lack of information
 - Objections from family members
 - Religious beliefs
 - Interference with funeral arrangements
- Must refer to the coroner:
 - Where death certificates cannot be signed
 - Thought to be related to an invasive procedure
 - ?Birth asphyxia
 - Deaths thought to be related to an instrumental delivery

Behavioural Issues

- Behaviour doesn't exist outside an environmental context

Behaviour Management

- History Taking:
 - Antecedent: what sets him off?
 - Behaviour: describe exactly what he does?
 - Consequence: What do you do about this?
- Principles:
 - Remove (time out). Somewhere safe and boring, and where you don't mind the child disliking (ie not the toilet if toilet training or bedroom if sleep training). Leave a minute for every year of age. Be specific about what they're going in for. At the end, remind of the behaviour you want, and then forget the incident.
 - Anticipate/avoid situations where conflict is likely
 - Ignore minor things, particularly tantrums
 - Distract
 - Example (set a good one)
 - Reward acceptable/wanted behaviour
- Reward Systems:
 - Star chart if young, more sophisticated and discrete if older
 - Agreed between parents and child. Child has to own it (can they help make it?)
 - Planned: don't have to make a decision when the time comes
 - Anticipated: known about in advance – **When** you this, **then** you will have ...
 - Consistently applied: no matter where he is or who he is with
 - Immediate: not at the end of the week or when dad gets home from work
 - Strong reward component
 - Meaningful to child:
 - Young child: cuddles, praise and attention
 - 8+ years: if you ... you can choose what we have for dessert/which video, etc (choice is powerful)
 - 10+: money
- Referral options:
 - Special Education Service (SES): Resource teacher for learning and behaviour (RTLB) or Behaviour Support Team through SES
 - Child psychiatry service (CAFS) if severe psychiatric symptoms (anxiety, depression, OCD, PTSD, sexually abused, ADD), persistent family dysfunction or resistant to simple management strategies
 - Paediatrician if medical issues
 - CYFS if abuse

Risk and Resilience

	<i>Good</i>	<i>Bad</i>
<i>Internal</i> (child factors)	Resiliency: High self esteem, happy temperament, high IQ, problem-solving skills, coping strategies, humour	Vulnerability: poor social skills, low IQ and self esteem, hopelessness
<i>External</i> (factors in the environment)	Protective: caring and supportive adult, reasonable structure and limits, being believed in	Risks: Family discord, hostility, lack of warmth and understanding, lack of friends

- Attribution theory: Are their successes and failures due to an internal locus of control ('I passed the test cause I did the work' → high self-esteem) or an external locus of control ('It doesn't matter if I study or not, it won't make any difference' → low self esteem)
- Individual traits that build resiliency:
 - Insight: recognition of ones' distressed condition with subsequent action to overcome barriers
 - Independence: gaining emotional distance and autonomy amid chaos
 - Initiative: achievements that foster self confidence and constructive activity
 - Relationship building: Protective and nurturing connections with at least one supportive adult
 - Creativity: facilities healing and positive activity in a difficult environment
 - Humour: focuses on hope not harsh realities
 - Morality: commitment to fairness and compassion
- Family traits that build resiliency:
 - Commitment: loyalty, determination to work things out, sacrifice for mutual benefit
 - Cohesion: togetherness, respect for the individual, interdependence
 - Adaptability: flexible, stress coping skills
 - Communication: listening and speaking skills
 - Spirituality: shared purpose and values
 - Connectedness: Support within and beyond family, attitude of service
 - Effective resource management: Competent use of money, time, etc
 - Coherence: Optimism and self reliance
- Intervention strategies:
 - Provide opportunity for and encourage contributions
 - Enhance decision making skills → ↑feeling of control
 - Encourage and give positive feedback
 - Develop self discipline: involve child in setting the rules and consequences

Toddler Behaviour

- Approach:
 - History, including:
 - Antecedents, behaviours and consequences
 - Social context
 - Collaborative history if necessary
 - Psychiatric history from mother (is the child the problem?)
 - PMH: ABFWIMPS
 - Exam: especially developmental
 - Education
- Most difficult behaviour does not indicate a serious disturbance. Indicators of serious disturbance include:
 - Deliberate self harm or messing
 - Wandering off
 - Running away
 - Age inappropriate sexual behaviour
- Developmental sequence of everyday habits:
 - Feeding
 - Sleeping
 - Eating
 - Toilet

- Going to bed and getting up
- Dressing and undressing
- Washing and cleaning teeth
- Aim is to achieve regular habits and routines:
 - To start with need to insist on regular routine and time schedule. Once achieved can be more flexible
 - Failure to achieve routine: daily hassle and distress
 - Regular routines → ↑security of child, ↓argument with parents
- Factors which ↓behaviour problems:
 - Routine and regularity
 - Clear limit setting
 - Unconditional love and affection
 - High level of supervision
 - Consistent care and protection
 - Age appropriate disciplines and rewards
- Tantrums:
 - Want their way. Purpose of tantrum is to get their way. Giving in reinforces the behaviour
 - Must be consistent. If you say no, will have to stick with it ⇒ choose your battles
 - Options for managing a tantrum (see Behaviour Management, page 570)
 - Ignore it: eg leave the room
 - Time out
 - Distract
 - Avoid problem areas (eg supermarkets)
 - Things will get worse before they get better. Once they realise the boundaries are consistent they will stop testing them
- Sleep Management: Sleep Management, page 593
- Other points:
 - Check parent's are not expecting too much of the child (eg 3 year old boy not wetting at night)
 - Keep no for important things
 - All parents make mistakes

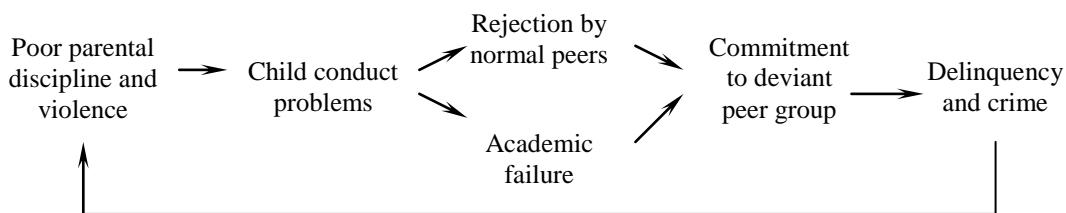
Problems at School

- For ADHD see Attention Deficit/Hyperactivity Disorder (ADHD), page 659
- Symptoms:
 - Normal IQ, no disabilities, but fail to develop academic potential
 - Difficulty with peer relationships, loners, act out, difficult behaviour
 - Develop associated problems: psycho-somatic, ↓self-esteem
- Usually multifactorial:
 - Constitutional factors: May have subtle defects in:
 - Receptive or expressive language
 - Auditory sequencing: can't remember verbal sequence (eg instructions). Can have a pervasive effect on schooling
 - Visual sequencing: difficulty reading/spelling
 - Motor problems (eg clumsy)
 - ↓Attention (may be secondary to the above)
 - Health, hearing, vision, etc
 - Environment: cultural, socio-economic status, family disruption, nutrition, etc
 - School related factors:
 - School factors associated with ↑antisocial behaviour: poor morale, high turnover, inconsistent standards, undervaluing children's work, bullying
 - Kids spend 15,000 hours at school – so can have a big impact (just as family does)
- Assessment:
 - History: parents
 - Information from teachers
 - Physical and neuro exam
 - Sensory exam: vision and hearing
 - Neuro-developmental, educational and psychological assessment
- For School refusal, see Separation Anxiety Disorder, page 661

- Management of Truancy:
 - Educational programme appropriate for the child's needs
 - Monitoring child through the day
 - Assist with the learning process

Child in Trouble with the Authorities

- History:
 - Interview child and caregiver separately
 - Presenting complaint
 - History of presenting complaint:
 - Describe behaviour: Antecedents, Behaviours, Consequences
 - Social Context in which behaviour occurs: Relationships within family, school, and peers.
 - Physical or sexual abuse
 - Collaborative history: parents, teachers, sports coaches – this is important
 - Psychiatric history: look for depression, anxiety, attentional problems
 - Formal assessment of learning if academic problems
- Exam: especially dysmorphisms, stature, neurocutaneous lesions, observations of reading, writing and relationship with parents, vision and hearing
- Development of antisocial behaviour:



- Possible differentials:
 - Attachment disorder
 - Developmental delay
 - Behaviour conduct disorder
 - Psychiatric illness: Depression, ADHD, PTSD (may appear to be daydreaming)
 - School refusal/Truancy
 - Neglect or other abuse
 - Domestic violence
- Management plan:
 - Keep in him school if at all possible: prognosis plummets if expelled or regularly truant
 - Ensure a thorough developmental assessment
 - Referral for psych assessment and counselling
 - Management: accentuate the positive, minimise the negative
 - Referral to other services

Attachment Disorder

- See also Anxiety Disorders, page 661
- Attachment:
 - Starts in utero and is an ongoing process
 - Securely attached infants:
 - Are able to seek and obtain comfort from familiar caretakers
 - Are willing to explore and master their environment
 - Insecurely attached infants (eg due to long separation from parents and multiple carer-givers in hospital) appear:
 - Anxious: clingy without obvious stress
 - Avoidant: angry, distrustful of parents, won't be comforted after brief separations
 - Indiscriminately affectionate: won't show preference for parents
- Concepts:
 - Separation: the process by which a child develops an identity separate from their parents. Promoted by secure attachment. At risk when the parents perceive the child is 'vulnerable'
 - Autonomy: Development of independence (→ social competence)

- Mastery: increasing sense of competence over the physical environment
- Together autonomy and mastery lead to an internal locus of control. Struggles for autonomy and mastery produce normal tantrums
- Types of Attachment Disorder:
 - Disinhibited type: will go to anyone. No stranger awareness and constant, insatiable need for attention. Likely to be due to neglect. Also see it in chronic hospitalisation
 - Withdrawn: frozen watchfulness, fearful. Likely to be due to abuse
- Test by observing child when parent leaves (separation), when a stranger comes in, and when parent returns (reunion)

Domestic Violence

- Has significant health consequences: injury, psychiatric, chronic pain, drug and alcohol abuse
- Is common (some studies report up to 20% of women being hit in the last year), but often missed by doctors
- Domestic violence starts with a cycle of increasing control and disempowerment. Violence is used to reinforce this
- Screening questions:
 - ‘I have seen many people who come to see me with problems like yours. In my experience, many of these women are being hurt in some way by their partner. Is that happening to you?’
 - ‘A lot of tension and violence can be due to relationships within the family – often with a partner. Is your partner being violent toward you?’
- Management:
 - Ensure mum and the children are safe. If not, refer to police/CYFS
 - Refer to Women’s refuge – be aware of the local services available
 - Educate: eg the cycle of violence, it won’t stop without help
 - Avoid victim blaming (‘it’s not your fault’)
 - Take careful notes (explain to the women why you are going this)
 - Display information in your waiting room – signals a willingness to discuss it

When Parents Separate

- Responses to parent’s separation – all signs of distress:
 - Withdrawn
 - Clingy
 - Regression
 - Difficult behaviour
- Helping the child:
 - Accept the separation – then the child will too
 - Make sure the child knows you love them
 - Avoid conflict in front of the child
 - Allow them to express their feelings
 - Rely on other adults not the child for support
 - Tell the kids they’re not to blame
- Things to avoid:
 - Don’t abuse their loyalty and trust
 - Don’t use them as messengers
 - Don’t use them to spy on other parent
 - Don’t continue to be angry at partner in front of them
 - Don’t let outings/gifts take the place of normal parenting
 - Don’t force kids to take sides
 - Don’t force a clash of loyalties

Growth and Development

Child Development

- Represents the interaction of heredity and the environment:
 - Heredity: potential of the child
 - Environment: extent to which potential is achieved. Requires:
 - Physical needs: warmth, clothing, shelter, food, health, activity with rest

- Psychological needs: security, personal identity, self-respect, independence, opportunity to learn, play, affection and care
- Areas of child development:
 - Gross motor
 - Fine motor
 - Language (expressive, receptive, non-verbal)
 - Social (interaction, play, self-care)
 - Cognitive: all of the above
- Requirements for development (need all of them):
 - Hardware (neurons, muscles, etc)
 - Motivation (often driven by frustration – a child can't do what it wants to)
 - Nurturing environment
- Types of assessment:
 - Developmental screening: point in time snapshot
 - Developmental surveillance: following over time
 - A formal assessment will yield a Developmental Quotient. $< 100 \Rightarrow$ delay. $100 \Rightarrow$ advanced.

Developmental assessment

- Indirect assessment of the acquisition of life skills
- Establish rapport: use names a lot, 'thanks for coming', etc → more valid assessment
- **History:**
 - Current development and time course of development
 - Order of questions should be:
 - When asking about milestones, start with things he is likely to be able to do and work up. Get better rapport than starting at the upper limit and working down
 - Hearing: What things can he hear?
 - Have you been concerned about his hearing?
 - What makes you confident of that?
 - Vision: What small things does he see?
 - Have you been concerned?
 - What makes you confident of that?
 - Gross motor: roll, sit, crawl, pull to stand, walk, run, scoot, pedal (progression: head → trunk → limbs)
 - Fine motor: pincer, feeding self, spoon, drawing, blocks
 - Expressive language: coo, babble, words with meaning, combinations (most common area of delay – usually focal not global)
 - Receptive language: Responds to familiar voice, to own name, one or two step instruction, knows name, gender, address, prepositions, pronouns
 - Social: smile responsively, laugh, stranger aware, play with peers, name friend
 - Self care: manage cup, spoon, undress, toilet, dress, laces
 - Get history of influences on development:
 - Miscarriages, still births
 - Pregnancy: toxins, alcohol, infections
 - Birth: APGAR (usually means brain was vulnerable before birth), gestation, birthweight
 - Neonatal congenital abnormalities, feeding, jaundice, infections
 - Early milestones (smiling, sitting, walking, first words)
 - Illness (eg CF, heart/renal disease, epilepsy)
 - Hearing (→ speech delay), vision (→ good verbal, poor motor)
 - Nutrition, constipation (especially if mobility problems)
 - Current development, especially social, self-care
 - Behaviour problems (sleep, tantrums)
 - Family stress
 - Family history, especially of development
 - History from other sources (eg kindy teacher)
 - Review previous rate of development: may get slowing before loss
 - Past Medical History: ABFWIMPS
- **Observation:** Look systematically across each of the 6 areas. Use toys as tools.
- **Examination:**

- On lap first (stranger shyness from 8 months)
- Dysmorphism: eyes, head shape, body proportions
- Height, weight, head circumference – plot them
- Vision (do first, affects motor): following, hundreds and thousands
- Localise to noise (do before language): if concerned then formal testing
- For each of gross motor, fine motor, expressive and receptive language, social and self care on the table below:
 - Ask open-ended questions to establish the floor (eg I notice he's walking, what other clever things is he doing)
 - Then use closed questions to establish a ceiling (eg can he walk backwards, throw over arm)
 - Then summarise: So he can but is not yet Have I got that right?.... Therefore he is at age X for that domain
- Summary: age for each domain is X, Y, Z. Therefore, overall, he's developmentally around age [Average for X, Y, Z]
- Other:
 - Skin pigmentation (eg tuberous sclerosis – seen under Woods lamp)
 - Ears, eyes, heart, abdomen, puberty
 - Neurologic exam
 - Relationship with parents
- **Plan:** for areas of weakness
 - If significant delay then early intervention
 - If some delay then anticipatory guidance – ‘what could you do to help’ – use Knowledge, attitudes/fears, practices, barriers framework
 - Always pitch safety advice at the level of gross motor skills

Development Chart: normal development from 0-60 months

- Ref: Dr Russell Wills
- Red flags:
 - Not smiling by 2 months
 - No eye contact by 3 months
 - Not reaching for objects by 5 months
 - Not sitting unaided by 9 months
 - Not walking unaided by 18 months
 - Not using words by 18 months
 - No 2 – 3 word sentences by 30/12 months

	Gross Motor	Fine motor-adaptive	Expressive language	Receptive Language	Personal-Social/Play	Self Care
6 wk	Clear face prone Follow O vertically	Follow 180 horizontal Follow O vertically	Cry, coo	Quiets to voice	Smiles spontaneously	
3 m	Up on elbows. No head lag on pulling up	Grasp Retain 1 block	Reciprocal vocalisation, laugh	Turn head to voice Localise bell/keys (horiz)	Reciprocal smiles	
6 m	Up on hands Sit supported	Take 2 blocks Transfer hand to hand	Consonants Mono-syllabic babble	Localise bell/keys (vert)	Lifts arms for pick up	
9 m	Sit stable Pull to stand Crawl	Object permanence: Take 3 blocks 1 at a time and hold onto them Bang, index point	Vocalise to communicate Poly-syllabic babble Jargon	Understands no, ta Localise bell/keys (diag)	Peekaboo	Cooperate with dressing
12 m	Move around furniture	Good pincer	Few words with meaning	Shake head for no Copy bye bye	Push toy car Clap hands	Independent with cup
15 m	Walk independent	Stack 2 blocks Mark paper with pencil, fist grip	Several words	Understands object names Wave bye bye on request Understands pointing	Push large wheeled toy Casting prom.	Remove item Indep with spoon
18 m	Walk backward Kick Throw over arm	Stack 3 blocks Vigorous straight scribble 3 shape board	Prom. jargon, two wants Many common objects Family names, own name	Few body parts Hands familiar named object on request	Symbolic play single step 21 mo: likes books Play alone	Remove hat, shoes, socks
2 yrs	Run Throw ball in bin Seat self at table	Imitate vertical line, then horizontal; dagger grip for pen Stack 6, train 3 3 shape board rotated	Combinations; Echolalia; Songs/rhymes 30 mo: Questions: what, who? 3-5 word comb; I, we, you Verbs: eat, kick, gone	Prepositions: on, in 2 step commands: shut door Object uses Several body parts; 30 mo: fetch	Imitative play single step 28 mo: ringaringarosy 30 mo: imit sequence	Indicate wet/dirty nappies Dress some
3 yrs	Walking: tandem, heels, toes Jump feet together Pedal; Up stairs adult	Stack 9, 3 stairs/bridge Imitate circle, cross, tripod grip 42 mo. Count bricks	Echolalia resolved Full name Plurals	Prepositions: under, up, down Mime complex gestures 42 mo: fetch several items	Imagine play seq Gender Name friend Share, turns	T-shirt Shoes and socks
4 yrs	Hop 3 steps/ Jump off 2 Catch big ball Down stairs like adult	5 brick gate 4 part man, ladder, square. Cut with scissors; Higher, longer	Intelligible to strangers Tenses Constant Qs: where, why...	Prepositions: between Opposites: big/little What would you do if?; Comparisons	Gives age Co-op play, hide n seek, snap Dressups, pretend	Undress indep.
5 yrs	Run up stairs Gallop Bounce and catch	6 part man, triangle, pencil grip 6 brick stair, castle Count 15 bricks	Grammatical sentences – conj. & except. Ask meanings of words	What things are made of: wood, metal Enjoy jokes, riddles	Knows address Names best friend	Dress indep.

- Older kids:
 - Gross motor: bike (can ride without trainer wheels at 5), sport (running, kicking), clumsiness
 - Fine motor: computer, play station
 - Cognitive: don't ask if does OK at school – everyone does OK these days! Instead, does he do age appropriate work, need extra tuition, etc

Cognitive Development

- Overall process:
 - Autonomy: dependent on parents → peers → independent
 - Abstract thinking (what if?): concrete → mature
 - Future consequences of present actions
 - Gratification: immediate → delayed
 - Satisfaction with body image
 - Black and white → comfort with shades of grey
- Infancy (birth – 2 years): Developmental issues:
 - Later develop goal directed activity
 - Learn to distinguish between self and surroundings
 - Develop object permanence
 - Need secure attachment relationship with parents
 - Separation, individuation in toddler years
 - At 2: trial and error problem solving, planned and purposeful play but limited content, egocentric, parallel play
- Preoperational (3 – 5 years):
 - Egocentric world view (I made it happen, so it's my fault)
 - Use of magical thinking, difficulty distinguishing real from symbolic (if I wish it, it will come true)
 - Trial and error problem solving only
 - One aspect of a problem at a time
 - Cannot order a series of events
 - Cause and effect thinking: I did X, then Y happened, therefore X → Y
 - Imaginative play
 - Gradually move from parallel play to interactive play with peers
 - Separation and autonomy
 - At 5: symbolic thought (imagination), classify by colour/shape, curiosity, magical thinking, social values, rules internalised but fixed, turn-taking, cooperative plan, other's perspective, increasing independence
- Concrete Operational (6 - 10 years):
 - Black and white thinking, right and wrong
 - Capable of simple logic and problem solving
 - Can order things in a chronological sequence
 - May have difficulties with multiple perspectives
 - Peer relationships increasingly important
 - Sharing games, competition
 - Analogy, metaphor, figures of speech being
 - Able to concentrate for longer, delay gratification, predict personal and social consequences of actions, plan ahead
- Formal Operations (10 – 13 years):
 - Better memory, concentration, forward planning
 - Social skills refined
 - Still concrete and literal (black/white, good/bad, right/wrong)
 - Limited abstraction: eg what if I didn't do this? (Contrary-to-fact abstraction)
 - Dramatic changes to body → constant comparisons and normal anxieties
 - Need to conform with peer norms
 - Difficult to take others perspective's
 - Difficult to understand complexity
 - Difficult to apply rules to own situation
 - Lack future orientation/forward thinking
 - Clear consequences
- Middle Adolescence (14 – 16 years):

- Developing abstract and complex thought
- Beginning to see other's perspectives, starting to cope with shades of grey
- Increased self consciousness
- Easily swayed – not certain of own view
- Still difficult to integrate conflicting ideas
- Narcissistic (feels good/what I want → therefore its right → impulsiveness)
- Less need to conform to peer norms, try alternative beliefs and philosophies
- Need limits to be secure, limit testing
- Late adolescence
 - Adult memory and concentration
 - Mature abstractions, problem-solving, self reflection and long range planning
 - Weigh up multiple information
 - See multiple meanings, complex relationships, different points of view, tolerant of shades of grey
 - Able to think hypothetically and plan for possible events
 - Remains more difficult to use new abilities in challenging situations
 - Autonomous: able to leave home and return for counsel, rely on own opinion

Developmental Delay

- Constant slow development leads to widening gap
- Investigations: hearing, vision, chromosomes, DNA screen (eg Fragile X, Angelman, Prader-Willi), thyroid, metabolic, mucopolysaccharide screen, CK (Duchenne's), brain imaging, EEG
- Type of Diagnosis:
 - Functional Diagnosis:
 - Mobility, communication, learning, self-care, socialising, etc
 - What does the child need to achieve age-appropriate function
 - Pattern diagnosis:
 - Autism: see Autism, page 582
 - Cerebral palsy: see page 629
 - Other syndromes
 - **Biological diagnoses:** DNA disorders, brain injury
- IQ scores:
 - < 20 profound intellectual disability
 - 20 – 35 severe
 - 35 – 50 moderate
 - 50 – 70 mild
 - 70 – 85 borderline
 - Definite or highly probable cause in majority < 50. Cause in about half < 70
- Management:
 - Objectives:
 - Maximising function
 - Preventing and treating secondary problems
 - Supporting carers
 - Referral: paediatrician, geneticist, psychologist (eg cognitive testing), SLT (speech, swallowing, play), physiotherapist (gross motor problems), OT (fine motor, self care, aids and equipment), early intervention groups, VNDT (Visiting Neurodevelopmental therapist), support groups
 - Medical assessment of a diagnosed, disabled child
 - Always consider new illnesses
 - Look for syndrome specific health problems
 - Feeding difficulties, nutrition
 - Constipation
 - Medication
 - Carer Stress
 - Access to services and allowances

Tamariki Ora (Well Child) National Schedule

- Covers:
 - Health education and promotion
 - Health protection and clinical assessment

- Family/whanau care and support
- Health education/promotion topics to cover at appropriate stages
- Prevention:
 - Types:
 - Primary: shifting the whole population curve → improves the overall standard
 - Secondary: identifying risk factors → early or targeted intervention
 - Tertiary: minimising impact of established disease
 - Benefits of prevention: ↓adult sequelae: injury, child abuse, delinquency and arrest rates
- PPV of parental concerns about delay is about 80–90%. Must act or refer on parental concern

Causes of Developmental Delay

- Causes of abnormal development:
 - Environmental
 - Genetic (eg chromosomal, metabolic)
 - Disability (vision, hearing, motor)
 - Brain injury (hypoxia, trauma, toxins, infection, prenatal & post-natal)
 - Illness, nutrition
 - Unknown

Hearing

- See Hearing Loss in Hearing Loss, page 151
- 1 in 500 has significant permanent hearing loss → receptive and/or expressive language delay
- All infants babble, even hearing impaired
- Suspect deafness when:
 - Parental concern
 - At risk babies (should be routinely screened):
 - Family history
 - Inter-uterine infection: rubella, CMV
 - Defects of ENT: cleft palate, external ear
 - Low birth weight
 - Neonatal distress
 - Poor response to sound
 - Not using words by 15 months
 - General developmental delay
 - Poor speech, comprehension and hearing failure
 - Following brain trauma, infection, neurotoxic drugs
 - Recurrent or persistent ear infections
- Normal development: See Development Chart: normal development from 0-60 months, page 576
- History:
 - Can he hear – how do you know?
 - Previous development: first word, use of consonants, etc. Check Well Child Book
 - Ear infections
 - Antenatal: rubella, prematurity, jaundice, drugs
 - Family history of hearing problems, developmental delay, neuro problems
- Exam:
 - Dysmorphic features: cleft palate, external ear, skin, heart murmurs, liver enlargement, normal genitalia
 - Basic neuro exam, gait, symmetry of movement (including face), eye movement
- Investigations:
 - Tympanogram
 - Don't do distraction testing – hard unless you're well trained. Send straight for audiology
 - Others depending on clinical findings: eg if regression then EEG, brain scan, check stressors, chromosome problems, CK for Duchenne's
- Differential of language delay:
 - End of normal range
 - Deafness
 - Isolated language delay (usually expressive more delayed than receptive – but not necessarily)
 - General delay or mild intellectual handicap → formal cognitive testing

- Autism
- Epilepsy: absence seizures – especially if fluctuates or regressive
- Possibly poor environment with little stimulation – but would also expect ↓socialisation and ↓self care
- Congenital problems: cleft palate, macroglossia (eg Down's)
- Rare isolated CNS or motor problems
- Management: Speech language therapist, early intervention service, multidisciplinary team if problems over other domains. GP to support and co-ordinate, anticipate problems – especially at transitions (eg school, moving) and checking for comorbidity (eg behavioural problems, ↓self esteem)
- Prognosis: Good if early intervention – but maybe problems with higher language function (eg essay writing)

Down Syndrome

- Trisomy 21: 47XY + 21
 - Accounts for 95% of presentations of Down Syndrome. Usually (80%) non-disjunction at first meiotic division
 - 5% have different karyotypes:
 - Mosaic Down: 3 %
 - Robertsonian translocation t14:21: 4.8%
- Epidemiology:
 - Overall incidence is 1 in 700
 - At least 20% still born
 - Incidence increases with ↑maternal age: at 16/40 gestation, 1 in 300 at 35 years, 1 in 22 at 45 years
 - Accounts for 25% of children with IQ < 50
 - ¼ of all chromosomal abnormalities. Chromosomal anomalies represent 15% of congenital anomalies
 - Risk:

Maternal age at birth	Down in live births
25 - 29	1:1100
30	1: 900
35	1:350
37	1:200
40	1:100
43	1:50
45 and over	1:25

- Neonatal Screening:
 - Only 30% of children with Down are born to women over 35. Widespread screening of those > 35 will have only minor increase in detection rate
 - Screening with the triple test will increase detection, but at the expense of significantly higher rates of invasive testing as there is a high false positive given the low incidence in younger women
 - See Prenatal diagnosis, page 360
- Neonatal signs:
 - Hypotonia
 - ↓Moro reflex
 - Joint hyper-extensibility
 - Excess skin at the back of the neck
 - Flat facial profile
 - Misshapen low set ears
 - Protruding tongue
 - Blunt inner eye angle
 - Single palmer crease in 50%
 - Clinodactyly (incurving) of little fingers in 50%
 - Big 'saddle' gap between big and 2nd toe
- Complications:
 - IQ generally from 45 – 55
 - Congenital heart malformations in ~50%: VSD, ASD, patent ductus
 - Susceptible to respiratory infections
 - Duodenal atresia
 - Also cataracts (2%), epilepsy (10%), hypothyroidism (3%), acute leukaemia (1%)

- Development:
 - Most will walk and develop simple language
 - Puberty is often delayed and incomplete
 - Average adult height is 150 cm
 - Pre-senile dementia (similar to Alzheimer's disease) supervenes after age 40
 - 8% live past 40 years

Autism

- Onset before age 3 of:
 - ↓Ability to form social relationships: slow to smile, don't enjoy being cuddled, indifferent eye contact
 - ↓Use of both verbal and non-verbal communication: slow onset, echolalia, no use of gesture, poor pragmatics (eg turn taking and eye contact in conversation). If it was isolated language delay you would expect compensation in other areas (eg social) but here that's affected as well
 - Restrictive and repetitive behavioural repertoire – dislike change
- May start from birth, or regress after normal development
- Other behavioural problems: outbursts, sleep problems, distractibility, poor toileting
- Rare: 2 – 4/10,000. Boys = 3 * girls
- 75% show some degree of general intellectual impairment
- Asperger's Syndrome:
 - Symptoms overlap with autism
 - Social interaction and behavioural problems similar to autism but not associated with significant language or intellectual delay

Effect of Chronic Disease on Development

- See also Chronic illness and disability in Adolescents, page 669
- 10 – 15 % of children have some chronic health condition. 1 – 2% are severe enough to interfere with their ability to take part in normal activities
- Chronic illness can effect development by:
 - Direct effect: eg deafness → language delay
 - Effect of treatment: eg neuro-radiation
 - Indirect effect: reduced energy in cystic fibrosis
 - Social environment: sense of differentness → withdrawal or bullying
 - Transaction: impact on parents (eg maternal depression) → affects child's adaptation
- May lead to failure to develop independence (self control) and competence (control over their environment), leading to self-doubt or indecision.
- Issues to consider:
 - Burden of care: don't give them more helpful ideas if they're already over-stretched!
 - Unpredictable future: Clear idea for the parent and child of what the future might hold
 - Social/school: Watch for 'vulnerable child syndrome', bullying, and access issues.
 - Cost: check relevant benefits received
 - Respite care: do parents need a break? Deal with feelings of guilt and indispensability
 - Activities of daily living: the daily routine will be revealing
 - Multiple professions: check these are co-ordinated and organised around the family's needs
 - Psychological: consider impaired attachment, depression, stress, family dysfunction
- Also ensure:
 - Information for child and parents
 - Access to services
 - Access to consumer groups
 - Equipment and transport needs
 - Environmental modification
 - Vocational training for an adolescent

Infants

- Effect on parents of congenital malformation:
 - Shock, disbelief, upset, problem solving processes slowed
 - Adaptation over time
 - Grief reaction similar to death of a child (must mourn the loss of a 'normal' child) – but parent must also attach to the living child

- Management:
 - Support good bond-enhancing practices before and immediately after birth:
 - Normal preparation for birth (learn about routines, processes, options, etc)
 - Time to establish rapport with paediatrician and visit NICU
 - Long periods together in first few days and breast-feed if possible. Is any separation really necessary?
 - Avoid criticism – a very sensitive time
 - Watch for signs poor attachment. See Attachment Disorder, page 573
 - For the toddler:
 - Watch for ‘vulnerable child syndrome’: continued parental concern after child has recovered → adverse affects on child. Problem is parents’ expectations, not attachment. More complicated when some ongoing vigilance is required
 - Support appropriate attitudes and plans
 - Mobilise family support
 - Remain optimistic
 - If in hospital, use separations to reinforce that parents will return. Limited number and consistency in nursing staff

Pre-schooler

- Social and emotional development may be limited through lack of opportunity to achieve goals in play and by limited peer interactions
- Management:
 - Refer for early intervention, especially low socio-economic and disabled children
 - Promote normal development: separation, appropriate discipline
 - In hospital: encourage rooming in, maximum contact with families
 - Warn parents to anticipate behavioural problems especially if hospitalisation is prolonged or frequent

Head injured child

- Initial crisis: grieving put on hold, waiting to see if things improve, child still looks the same, swinging between hope, despair and disbelief
- Restructuring:
 - Reassign tasks in the family
 - Move out of crisis reorganisation into long term reorganisation
 - Inclusion of outside help into family
 - Appropriate time for husband/wife/other children
 - Time for self
- Grieving:
 - Allow for grief and acknowledge the loss
 - Avoid dichotomy of one person (eg mother) taking hope position and others despair
 - Promote openness. Devastation of silence
 - Denial can also be a coping mechanism
- Develop an acceptance of a new identity through the crisis:
 - Seeing how the child is different
 - Finding positives in this new identity and helping the family value these
 - Achieve a sense of movement through the crisis. Mark positives and achievements of the family
- Encouraging compliance:
 - For the highly compliant: teaching, directions
 - For the non-compliant (those who respond ‘yes – but....’): general indirect messages, metaphor/story telling
- Subsequent learning disabilities: may have problems with learning from then on – but may not show up till those skills are needed (eg trouble reading when they start school)

Learning Disability

- History:
 - Start with things he is likely to be able to do and work up
 - Questions over traditional domains for learning:
 - Reading: ‘what is she reading now’, ‘can she read three letter words’
 - Spelling

- Numeracy
 - Writing
 - Drawing, art, craft
 - Social skills
- Strengths
- Collaborative history:
 - Previous assessments, IQ tests
 - Talk to the teacher
- Comorbidity screen:
 - Is the norm in developmental paediatrics
 - Can be:
 - Primary: eg biological morbidity such as learning and co-ordination difficulties, ADHD and clumsiness
 - Secondary: eg acquired psychological and behavioural problems such as loss of self-esteem, non-compliance, etc
- Differential:
 - Behaviour: aggression, attention seeking, school refusal
 - Mood, anxiety, attention
 - Relationship with peers, teasing, bullying
 - Family issues – get good social history
 - If adolescent then HEADDSS assessment (See page 666)
- School factors: teacher skills, interest/ability to manage the child's needs, available skills
- Parental insight: are they helping or hindering
- Use questionnaires: eg Child Behaviour Checklist (screen for anxiety, depression, etc) or Connor's (specific for ADHD) to provide diagnostic information and provide a pre-treatment baseline
- Exam:
 - Screen for gross and fine motor delay
 - Refer for vision and hearing tests
- Possible differentials:
 - Hearing and vision
 - Medical: hypothyroid
 - Intellectual disability
 - Specific learning disabilities
 - Head Injury
 - Psycho-social: Abuse, stress, etc
 - Psychological: depression, anxiety, ADHD
- Principles for management:
 - Review and follow-up (eg 3 monthly), especially at times of transition (eg changing schools)
 - Multidisciplinary approach: OT, Physiotherapist, SLT, VNDT, Educational Psychologist
 - Excellent communication between professionals
 - Helping parents to create realistic goals
 - Dealing with normal parent grief
- Strategies for management:
 - Demystify: Explain strengths and weaknesses to the child, parents and teacher. Removes guilt, pejorative labels (eg lazy), gives optimism
 - Bypass strategies: adjust rate, volume, complexity, format or use devices to make the task easier
 - Remediation of skills: focus on study skills, organisation, use strengths to remediate weaknesses
 - Developmental therapies: Eg speech therapy, gross and fine motor, etc. More effective when skill deficits reflect lack of opportunity, and when instituted earlier
 - Modify the curriculum: Eg drop subjects they're not succeeding in
 - Strengthen strengths: sport, art, mechanics, etc
 - Individual/family counselling: especially with behaviour management, family dysfunction
 - Advocacy
 - Medication
 - Longitudinal case management
- Check whether parents get the child disability allowance. Can get a needs assessment done for respite care, home help, etc

Child Development Team

- For children with:
 - An identified disability
 - Developmental delay
 - At risk of developmental delay/difficulties
- Involves multi-disciplinary assessment and intervention
- Social Worker:
 - Conducts individual, marital and family social assessments
 - Liases with other community services (CYFS, WINZ, etc) and facilitates brokerage of services
 - Provides emotional support
 - Teaching parenting skills
 - Advocacy
- Psychologist:
 - Assessment: neuropsychological, development, behaviour/emotion, family function
 - Intervention: For individual, skills for parents, family relationships
- Physiotherapist:
 - Functional assessment of gross motor skills: delay, abnormal muscle tone, loss of range of movement, gait abnormalities, mobility, co-ordination
 - Therapy (including hydrotherapy) and home/school exercise programmes
 - Assessing for standing frames, walking aides and wheelchairs (with OT)
- Occupational therapist:
 - Assessment of fine-motor skills (use of hands):
 - Tool manipulation: grasp and grip, bilateral hand use, release, eye-hand co-ordination (eg stacking)
 - Pre-writing: lines, circles, picture of a person
 - Handwriting: grip, control, sizing, closure, hand dominance, speed
 - Cutting with scissors: accuracy and co-ordination
 - Assessment of self-care skills:
 - Undress/dress, buttons, zips, shoelaces, etc
 - Feed themselves
 - Sit unsupported in the bath
 - Toileting, including sitting on toilet, pulling pants down, wiping
 - Clean teeth, brush hair, wipe face
 - Assess for equipment to help with the above
- Speech language therapist: assesses and assists with:
 - Receptive language: understanding
 - Expressive language: including gesture and facial expression
 - Phonology: sound system
 - Pragmatics: social rules – sharing, turn taking, eye contact (biggest problem in autism)
 - Feeding: transition from tube to oral feeding, behavioural feeding issues
 - Voice: vocal nodules due to abuse (eg screaming)
 - Fluency: stammering
- Visiting Neurodevelopmental Therapist:
 - Home based assessment
 - Family support
 - Liaison with other health professionals and community agencies
 - Assessment for equipment
- Developmental paediatrician:
 - Developmental assessments/examination for suspected delay
 - Investigates cause
 - Review of developmental progress

Growth

- Growth velocity = change in height over time. Declines till about 4, levels out, spike at puberty then zero
- Factors influencing growth:
 - Genetic potential
 - Psychosocial factors (eg psychosocial dwarfism)

- Nutrition (including in utero): adequate calories, balance of nutrition
- Diseases in major systems: uses energy (eg ↑ respiratory effort) and nutritional effects (eg GI)
- Hormones and Growth factors
- Measurement:
 - Method: Use stadiometer, fixed to wall, feet together, knees straight, lift mastoid processes
 - Accuracy and reliability:
 - SD of a single measurement ~ 0.25 cm. In a 5 year old this can cause a range in growth velocity from 10th to 50th centile
 - Taller in morning than at night
 - Minimising error: Same measurer, calibrate regularly, careful measurement, don't look at last measurement, measure at beginning and at end of exam

Short Stature

- Definition:
 - > 2 standard deviations below the mean = below 5th centile
 - Reduced growth velocity
 - Exclude failure to thrive
 - Growth pattern is more important than height
 - Normal variants:
 - Familial (genetic) short stature
 - Constitutional delay of growth and development. Presents mid to late childhood
- | | Familial (genetic) short stature | Constitutional Delay |
|----------------------|----------------------------------|--|
| Height | < -2 SDs | < -2 SDs |
| Bone age (hand xray) | = Chronological | < Chronological. Delayed through childhood, accentuated when peers reach puberty |
| Puberty | Normal | Delayed |
| Growth velocity | Normal | Normal |
| Final height | Short | Normal/Tall (keep growing for longer) |
| Parents | Short | Normal |
| Family History | Positive (for short stature) | Positive (for constitutional) |

- Pathological causes:
 - Systems: eg subclinical GI or renal disease (reflux, coeliac, malabsorption, CF, etc)
 - Psychosocial
 - Genes:
 - Turner syndrome: webbed neck, wide nipples, wide carrying angle
 - Skeletal dysplasia: eg achondroplasia
 - Syndromes
 - Hormones: Thyroid or GH deficiency, glucocorticoid excess
 - Drugs: Steroids
- Assessment:
 - History:
 - Height: measured accurately and over time
 - Mid-parental height: assessment of genetic potential (adjusted so both parents are same sex as child. Male = female + 13 cm or average their centiles)
 - Family history: eg constitutional delay
 - Systems
 - Psychosocial
 - Development
 - Examination:
 - Growth parameters
 - Dysmorphic features → ?syndrome
 - Proportions: limbs vs trunk, eg arm span vs height, or upper segment (head to pubic bone) vs lower segment (pubic bone to floor)
 - Blood pressure (?renal disease)
 - Fundi and visual fields (?pituitary tumour)
 - General
 - Investigations:

- Bone age: accurate to about 3 months
- Specific depending on history/exam, eg renal → creatinine, coeliac → antibodies
- Karyotype in girls
- Treatment:
 - Treat cause
 - Growth hormone:
 - Effective in GH deficiency and Turner's syndrome
 - May help in chronic renal failure, intrauterine growth retardation and severe idiopathic short stature
 - Androgens: consider in constitutional delay – won't influence final height but get there faster.

Tall Stature

- Arbitrary definition
- Associated stigma (females more often seek help)
- Causes:
 - Familial/genetic
 - Over-nutrition
 - Syndromes (eg XXY, Marfan's, Homocystinuria)
 - Precocious puberty (tall early, but stop growing → eventually short)
 - Growth hormone excess is extremely rare

*Growing Pains **

- Occurs frequently: 15% of children with peak age of 11
- Diagnosis of exclusion – no organic pathology usually found. ?Child more vulnerable to pain and stress-induced exacerbations
- Occurs at least monthly for a three-month period. Between times the child is well
- Differential:
 - Orthopaedic disorders
 - Collagen vascular disease
 - Infection
 - Neoplastic disorders
- Management:
 - Reassure, even if you can't find a cause
 - Symptom diary (also check for psycho-social stressors)
 - Symptomatic relief

Neonatal and Infants

- Neonatal is < 4 weeks

Examination of the Newborn

History

- Maternal history:
 - General health and well-being: past medical history and social history (partner, planned pregnancy, etc)
 - Pregnancy: medications, alcohol and other drugs, complications, infectious illness (toxoplasmosis, rubella, etc), EDD, scan findings, parental blood groups
 - Family history: perinatal deaths, paediatric deaths, congenital problems (especially congenital dislocated hip)
 - Delivery history: length of labour, infection, resuscitation, APGAR, any concerns
 - Post-natal history: feeding, colour changes (blue, jaundice), behaviour, stools, urine
 - Have you any concerns about your baby?

Examination

- Initial assessment immediately after birth to check adaptation to extra-uterine life (eg APGAR) and to look for major congenital anomalies, especially:
 - Dysmorphic features
 - Choanal atresia
 - Major limb defects

- Spina bifida
 - Anal atresia
 - Genital abnormalities
 - Birth trauma: bruising, cephalhaematoma
- Examine on Resuscitare. Check all equipment carefully first.
- APGAR assessment – at one minute, then 5 minutes then every 5 minutes till a score of 10:
 - Heart rate: 2 for > 100, 1 for < 100, 0 for not present
 - Colour: 2 for pink, 1 for blue, 0 for pale
 - Respiration: 2 for regular or strong cry, 1 gasping intermittently (may be bad sign – secondary hypoxia), 0 for none. May slow due to maternal drugs (eg pethidine)
 - Tone: 2 for active movement, 1 for limb flexion
 - Response to stimuli: On suction, 2 for coughs well, 1 depressed
- Apnoea:
 - Primary Apnoea: pulse < 60 and cyanosis. Give O₂ and wait a minute
 - Secondary Apnoea: pulse < 60, pallor and floppiness: suction, ventilate, intubate
- General inspection:
 - Dysmorphisms: eyes, ears, mouth, cry
 - Colour: central, peripheral
 - Respiratory effort: grunting, indrawing, flaring nostrils
 - Posture and movements:
 - Normal: hips abducted, partially flexed, knees flexed, arms adducted, flexed at elbow, hands closed (not tightly), fingers over thumb
 - Abnormal: hypotonia, irritability
 - Skin: colour, rashes
- Systemic examination:
 - Head:
 - Skull: fontanelles, sutures, birth trauma
 - Eyes: red reflex, opacities, conjunctivitis
 - Nose: patency
 - Mouth: palate and suck
 - Ears: hearing, tags
 - Neck: upper airway
 - Chest: shape, deformities, respiratory distress, cardiac auscultation, peripheral pulses, respiratory auscultation
 - Abdomen: cord, 3 vessels (2 arteries and a vein), shape, liver, spleen, kidneys, bladder, genitalia, urine stream, anus, passage of meconium, femoral pulses,
 - Limbs and other bones: upper limbs, digits, palmar creases, clinodactyly, grasp, lower limbs, digits, hips, talipes (club foot), spine
 - Neurological status: cry, jittery, spastic, grasping, activity, irritability, symmetry of movement, tone, neonatal reflexes
 - Neonatal reflexes: stepping, walking, Moro, grasp, rooting
- Also:
 - Growth: weight, length, OFC → plot
 - Offer vitamin K IM as prophylaxis against Haemorrhagic disease of the new born
 - Cord blood for blood typing and Rhesus -ive, and also measure Cord pH (from artery) – measure of hypoxia
 - If baby has patches of yellow ⇒ sitting in meconium for a while → stain
 - If uncertainty about gestational age then formal assessment
 - Re-examine at end of the first week of life, especially for signs of congenital heart disease. Takes ~ 48 hours for ductus to close
- Other observations:
 - Micturition: usually soon after birth, infrequent for first 24 hours
 - Bowel: 99.9% passed meconium by 48 hours/ Otherwise ? Cystic Fibrosis, Hirshprungs
 - Jaundice: 40% develop it, but transient, resolves by day 5
 - Vomiting: a little is common. Green is bad (= bile)
 - Temperature: rectal best. Same range as adults when dressed appropriately
 - Weight: 1st 3 – 5 days may lose 5 – 10% of birth weight. Should regain it in 7 – 10 days
- In first week:

- Immunisations: if mother HBsAg +ive then Hep b Vaccine and HBIG
- Guthrie card. See Genetic Testing, page 465

Outcome after Preterm Birth

- At 27 weeks, 90% survive to discharge
- Definitions:
 - Prematurity: < 37 = weeks Preterm, < 33 = weeks Very preterm
 - Birth weight (?relevance to Pacific Island Babies – usually heavier):
 - < 2.5 Kg: LBW
 - < 1.5 Kg: VLBW
 - < 1.0 Kg: Extremely low birth weight
- Factors affecting prognosis:
 - Prenatal: Socio-economic, maternal smoking, infertility
 - Antenatal: multiple birth, IURG, maternal illness, smoking, steroids before delivery
 - Birth: time of transfer, method of delivery, APGAR, resuscitation
 - Postnatal:
 - Size of NICU, surfactant, breast feeding
 - Hypoxic-Ischaemic Encephalopathy (HIE): ↓O₂ delivery to brain → becomes oedematous over next 24 – 48 hours
- Assessment of outcome: lots of problems with cohort studies: which population, admission, length of follow-up, what's measured, etc
- Issues for mothers of NICU babies:
 - How they perceive health workers
 - Postnatal Depression
 - Visiting family commitments
 - Breast feeding: often expressing

Complications of Preterm Birth

- Anaemia:
 - Miss out on the ‘iron loading’ that happens through 3rd trimester
 - Haemorrhage: feto-maternal, twin to twin, placental, cephalhaematoma, etc
 - Haemolysis: Rhesus disease, ABO incompatibility, spherocytosis, G6PD deficiency
 - Infection: CMV, rubella, septicaemia, UTI
 - Bleeding disorder: haemorrhagic disease of the new born
- Respiratory Distress Syndrome:
 - =Hyaline Membrane Disease
 - Inversely proportional to gestational age and birth weight, also diabetic mothers, asphyxia, cold stress, etc
 - Surfactant deficiency → alveolar collapse → haemorrhage/protein leaking → hyaline membrane
 - Signs: indrawing and expiratory grunt
 - CXR: ground glass appearance with air bronchogram. See Chest Radiology, page 604
- Broncho-Pulmonary Dysplasia (BPD):
 - Follows ventilation for respiratory distress and O₂ toxicity
 - Histology: necrotising bronchiolitis and alveolar fibrosis
 - Mortality 40%
 - Long term: airways obstruction, airways hyper-reactivity and hyper-inflation
 - CXR: patchy collapse and fibrosis with areas of cystic change and over-distension
- Intraventricular Haemorrhage (IVH): small haemorrhages into the germinal layer lining the lateral ventricles with hypoxia. May → hydrocephalus. Most have no serious long term sequelae
- Parenchymal Haemorrhage:
 - Into brain, not IVH
 - Incidence 1 – 2 % of preterms
 - Most are unilateral
 - Outcome depends on site
 - Varies from nil to severe hemiplegia
- Periventricular Leukomalacia:
 - Incidence 4% of preterms
 - ?Associated with maternal infection

- Frontal, usually watershed lesion
- Cysts long term → spastic diplegia (legs worse than arm)
- Retinopathy of Prematurity: Abnormal vascularisation of retina following exposure to high O₂ concentrations. Screen all babies < 31 weeks or 1500 g
- Necrotising Enterocolitis:
 - During first 3 weeks (up to 3 months in VLBW infants). Rare in term babies
 - Aetiology uncertain:
 - Hypoxic damage to bowel wall (?umbilical catheterisation, apnoeic spells, septicaemia)
 - Colonisation with certain bacteria: Clostridium perfringens, E Coli, S Epidermidis, Rotavirus
 - Necrotic segment of intestine with Pneumatosis Intestinalis ('string of pearls' sign on X-ray plus portal gas seen in liver) → perforation, sepsis, etc
 - Presentation: sepsis, bloody stools, bile stained vomiting
 - Pathogenesis:
 - Necrotising inflammation of the small and large intestine
 - Mucosal oedema → necrosis → gangrene, perforation, peritonitis
 - Sequalae: malabsorption, strictures, short bowel syndrome
- Skin easily irritated (eg alcohol, tape, drips) → long term scars
- Also:
 - Jaundice more common
 - Hypoglycaemia more common
 - Failure of closure of patent ductus (give anti-PGs, eg endomethacin)
- Problems associated with Intrauterine Growth Retardation:
 - Immediate:
 - Hypoglycaemia (see Hypoglycaemia of the New Born, page 595)
 - Polycythaemia (eg due to placental insufficiency) → heart failure (due to ↑viscosity), pulmonary hypertension, NEC. Treat with exchange transfusion (eg or saline) → ↓Hb
 - Hypocalcaemia (test ALP)
 - Jaundice
 - Plus others (eg Cerebral Palsy)

Neonatal and Infant Anticipatory Guidance (Parent Education)

- See Parent and Adolescent Education, page 567
- Consider the topics for discussion about a neonate:
 - Vision and hearing: Can your baby hear and see (how do you know?)
 - SIDS prevention: sleep on back, ↓smoke exposure, breast feeding, nothing over head when sleeping (see Sudden Infant Death Syndrome (SIDS), page 594)
 - Immunisation: the schedule, genuine and non-genuine contra-indications, common myths, benefits and risks (see Vaccination Practice, page 517)
 - Maternal mental health: screening and assessing for post-natal depression (See Postpartum Mood Disorders, page 430)
 - 6 week screening: dysmorphic features, cleft lip and palate, growth, eyes, heart, hips (see Six Week Check, page 374)
 - Contraceptive advice
 - Smoke cessation
 - Always ask why has the mother *really* presented
- When neonatal and/or later, consider the following:
 - Recognition of illness, emergency contacts
 - Feeding: breast feeding and maternal nutrition, introducing solids, nutrition
 - CPR
 - Parenting skills: eg management strategies for sleep and toddler behaviour, toileting, eating
 - Injury prevention: seat belts, fire safety, falls, hot water, sun exposure, poisoning, safe child care, pools, playgrounds, road
 - When to expect which developmental milestones. Reassure for parents. Also early identification → early intervention
 - Developmental needs of kids: play, language, nutrition, social etc

Breast-feeding

- See also Pharmacology of Pregnancy and Breast Feeding, page 528

- See also Breast in Pregnancy and Breastfeeding, page 376
- Advantages:
 - Prevention of disease: passive immunity against gastro-enteritis and ↓otitis media due to better Eustachian tube drainage
 - Bonding
 - ↓PPH
 - ↓SIDS
 - Cheap and convenient (available, portable, sterile – cf bottle feeding, especially in 3rd world)
 - Contents vary with circumstances (fore milk has ↑ water content)
 - No constipation
 - Less spilling, less irritating than bottle feeding
 - Supply matches demand
 - Smells nicer at both ends. No constipation with breast milk
 - ?Higher IQ
 - Males can't do it!
- Disadvantages:
 - Discomfort establishing
 - Limits mum
 - Limited iron and phosphate, Vit D and C if preterm (cf bottle feeding which can be fortified)
 - Can't easily measure intake
 - Leaking
 - Maternal drugs are included (eg lithium)
 - Breast milk jaundice
- Establishing breast feeding:
 - Babies don't feed much for 1st 48 hours
 - Breast milk comes in around day 3 (especially 1st baby) ⇒ baby's hungry on day 3
 - Can hurt – usually uncomfortable
 - Growth is best way of proving adequacy
 - Very hard to overfeed compared with bottle feeding (sucking is a reflex → will keep bottle feeding even if they don't want the feed)
- Ongoing issues:
 - If feeding too regularly then baby will be getting CHO rich foremilk but not fat rich hind milk → hungry
 - Attachment to the breast is key: Is the baby nipple feeding or breast-feeding. If nipple then repeated trauma → pain, cracked nipples, etc
 - Mastitis or blocked duct → express lots (try it in the bath)
- Establishing bottle feeding:
 - Day 1: average intake 60 ml/kg (= 40 calories/kg)
 - ↑ by 15 ml/kg/day until average of 150 ml/kg/day
 - If too much then ↑ stools, ↑ vomiting, ↑ misery
 - Alternatives to cows milk: goat (but no folate), soya, hydrolysed (if allergic to everything else)
 - Allergy: eczema reaction mainly to casein proteins, but can also be allergic to whey protein
 - Can be intolerant (ie non allergic reaction) to:
 - Lactose (galactose + glucose): ↓lactase → osmotic diarrhoea + ↑fermentation by bacteria → ↑gas → frothy acid stools → acid burns round perianal skin. More common as secondary intolerance (eg following Rotavirus). Breast milk has lactose too.
 - Fructose (eg fruits)
 - Sorbitol (artificial sweeteners)

Failure to Thrive (FTT)

- = Failure to gain weight normally (< 3rd percentile, or falling serial measurements) [cf Stunted growth = failure to gain height]
- If also failure of linear growth ⇒ long standing problem (weight always falls first, then length, then head circumference falls last)
- History:
 - What goes in (diet):
 - What and how much (and does it actually go in, or is it just offered?). Milk, other drinks, meat, fruit and vegetables, cereals and breads, lollies

- Assess parents knowledge base
- Feeding difficulties: appetite, behavioural, structural, swallowing
- What comes out (poos) – especially steatorrhoea. People usually overestimate vomit
- Chronic illness: cardiac, renal, neurological
- PMH: ABFWIMPS
- Development
- Social history: especially PND, other psych stresses, violence, drugs and alcohol
- Examination:
 - End of bed: fat, thin, energy, pallor, well/sick, dysmorphisms
 - Muscle and fat stores – look for scraggy buttocks
 - Signs of abuse and injury
 - Signs of chronic disease:
 - Cyanosis due to heart: L → R shunt *and* heart failure or cyanotic lesion (R → L shunt)
 - Respiratory: clubbing, nasal polyps (CF, asthma)
 - Gut: coeliac (not if breast feed) – distended abdomen and thin legs
 - Renal: blood pressure
 - Assess suck, chew, swallow
 - Rickets (\downarrow vitamin D), anaemia (\downarrow Fe), Bruising (\downarrow vitamin K), dermatitis & neuropathy (\downarrow Vitamin B) (all late signs)
- Differential:
 - Parent's expectations: In the 2nd year of life: \downarrow appetite, \downarrow rate of growth, \uparrow activity are all normal. Parents may need reassurance
 - Non-organic failure to thrive:
 - Inadequate parenting/poor nutrition the most common cause (will feed and gain weight well while in hospital).
 - Usually complex situation: eg young mum, unwanted pregnancy, obstetric problems, poor bonding, bottle feed, maternal depression, etc.
 - Is the milk being made up properly, any strange stuff (eg tea, Milo, etc)
 - To check for attachment: observe mum chatting to baby while they dress – is she talking to the baby
 - Organic causes:
 - \downarrow Intake secondary to:
 - Underfeeding (eg engorged breasts → poor latching on, inverted nipples)
 - Congenital abnormalities (eg cleft palate)
 - Dyspnoea (eg chronic heart failure, CF, chronic URTIs)
 - Neurological lesions (eg pseudobulbar palsy)
 - Behavioural factors (eg alert, restless)
 - Abnormal losses:
 - Vomiting: need to be severe and persistent to → FTT. Eg pyloric stenosis, chronic UTIs, renal disorders
 - Stools: diarrhoea, steatorrhoea
 - Urine: eg diabetes, renal failure, diabetes insipidus, adrenal insufficiency
 - Failure of utilisation:
 - Chronic infection (eg Tb, UTIs, immune disorders)
 - Metabolic disorders (eg phenylketonuria)
 - Endocrine disorders (eg hypothyroidism)
 - Constitutional and genetic abnormalities: Short stature, Down's, Turner's, Achondroplasia
 - Increased requirements: Chronic lung disease, heart disease, etc
 - Macrosomic babies (ie mum diabetic) will lose excess weight after birth → looks like failure to thrive
- Management:
 - If non-organic failure to thrive, then educate regarding a baby's dietary needs. See Parent and Adolescent Education, page 567
 - Investigations: rarely necessary. Maybe Fe for anaemia

The Crying Baby

- A multifactorial problem
- Normal crying:

- Babies cry their most at 6 weeks – just when the honeymoon period is over and all the supports have gone back to work/gone home
- Range for $\frac{1}{2}$ to 7 hours per day
- It's their only means of communications
- May be hungry, overfeed, tired, pain, bored, hot, cold, inadequate burping, switching breasts too soon (\rightarrow low fat feeds), solids before 3 months.
- Note especially babies cry when they're tired – common mistake is to stimulate and sooth them when they need to sleep
- Not due to parental stress. Crying leads to stress not the other way round. Harder for older women and professional who worked up to delivery to cope with ($\rightarrow \uparrow$ sense of isolation post delivery)
- Colic: definitions vary from crying lots to “well thriving baby who develops muscle spasms, flushing face, pulls up legs, screams. On and off every few minutes for several hours, loud tummy rumbles, relieved by flatus or passage of stool”
- Theories:
 - Gut immaturity \rightarrow disordered intestinal motility \rightarrow GI pain
 - CNS immaturity \rightarrow immature, disorganised response to stimuli \rightarrow response to most things is to cry
 - Very unlikely to be lactose intolerance (rare before 3 months) or maternal cows milk consumption
- History:
 - Clarify what the parent wants to know – address their issues
 - HPC: How often, when, associated behaviours, timing, pattern
 - Vomiting and bowel patterns
 - Feeding and sleep patterns
 - PMH: ABFWIMPS
 - Maternal social history: attitude to baby, supports, PND, drugs and alcohol
- Exam and investigations:
 - Check growth
 - Exclude physical causes:
 - Acute: otitis media, intestinal cramping/diarrhoea, corneal abrasion, incarcerated hernia
 - Chronic: gastro-oesophageal reflux
 - Nutritional intolerances from mother's diet (rare)
- Issues:
 - Baby's safety: Is mum is at breaking point?
 - Feeding problems: sore nipples, nipple infection (eg thrush)
 - Maternal mental state: depression, lacking support, sleep deprived, anxious
 - Maternal nutrition: is she eating well?
- Management:
 - Acknowledge strain
 - Reassurance: “I have looked carefully for physical causes and there are none that I can see”. “Baby is growing well so is getting the food they need”
 - Things to try: rocking, pram, vacuum cleaner, ride in car, dummy, massage, warm bath
 - Feeding: not too often, burp well, having enough?, no solids till 4 – 6 months, maternal diet (\downarrow caffeine, cabbage, onions, experiment with what causes baby to cry)
 - Optimistic outlook: from 6 weeks to 3 – 4 months amount of crying normally reduces significantly
 - Active advice: plan what mum can do to make it easier
 - Referral to Plunket nurse or Plunket Karatane centre and/or lactation consultant

Sleep Management

- Principles:
 - Sleep is a learned process – you train your baby to do it
 - After 6 months a night feed becomes a reward for waking up \rightarrow trained night waker
 - Parents also need time for themselves
- For babies:
 - Night feeds: quick, quiet, dim light
 - Leave the baby to cry for a while
 - Wrap them well, then not woken by their own reflexes (eg startle reflex when lightly asleep)
- Toddlers:

- Evening routine: won't harm toddler if you're firm with bedtime routines. No energetic games beforehand
- Approach to Sleep Training:
 - Agree with partner/family what you are going to do
 - Plan in advance (eg start on a long weekend). Warn neighbours
 - Tell the child how it is going to be and why
 - Quiet bedtime routine every night
 - Put in bed, say good night, walk out
 - If they come out, return them to bed with no reinforcement or eye contact
 - If they cry, wait 5 minutes, then 7 minutes, then 9 minutes, etc. When going in, no reinforcement
 - Stick with it. May get worse before it gets better. Should see improvement by 5th night

Sudden Infant Death Syndrome (SIDS)

- Defn: death < 1 year, and still unexplained after autopsy, review of clinical history and examination of the death scene (in practice none of these is usually done well)
- Epidemiology:
 - 1990: approx 4.5 per 1000 live births
 - 2000: approx 1 per 1000 live births (about 70 per year). Pakeha lower, Maori about 4 per 1000
- Epidemiological risk factors:
 - Age (3 – 5 months)
 - Maternal smoking – now greatest modifiable risk factor given sleeping on back well established
 - Prone sleeping position
 - ?Bed sharing
 - Seasonal (winter worse)
 - Previously well
 - Race (eg higher in indigenous minorities)
 - Male
 - Low birth weight
 - Low maternal age
 - Low Socio-economic status
- Theories:
 - Re-breathing of expired gases (eg prone or bed sharing)
 - Hyperthermia
 - Co-sleeping (bed sharing)
- Differential diagnosis:
 - Child abuse (eg shaking injury, suffocation)
 - Metabolic disease
 - Cardiac disease (congenital or acquired)
 - Overwhelming sepsis
 - Accidental asphyxia (eg in bed) – requires good death scene exam and history
- SIDS follow-up:
 - Explanation of death
 - Explanation of grieving process
 - Follow up with next child
 - Screen for risk factors
 - Role of monitoring (no evidence of effectiveness but reassuring for parents)
- Prevention:
 - Supine sleep position
 - No smoking
 - Own cot
 - Avoid bed sharing or sofa if tired or smoker or alcohol intake or pillows
 - Dress for room temperature (ie don't let them get too hot, no hat in bed)
 - Make up bed so they can't slip under the covers (ie short-sheet the bed)
- Complications of prone position: Plagiocephaly (flat spot on skull). Prevent by varying position of the head when lying

Neonatal Acute Airway Problems

- Choanal Atresia: failure of formation of nasal passages. Baby goes blue until someone opens the mouth. Can't pass NG tube. Can be unilateral
- Congenital masses: nasal encephalocele and nasal dermoid. Care with nasal intubation. Beware the midline lesion
- Pierre Robin Sequence: short jaw, cleft palate and tongue falls back and obstructs. Nurse prone. Associated with oligohydramnios
- Subglottic Stenosis: due to intubation trauma in a preterm baby

Hypoglycaemia of the New Born

- Not a big deal, but needs to be recognised and managed
- Causes (either big babies or small babies):
 - Hyperinsulin: Child of poorly controlled diabetic mother. ↑Maternal glucose → ↑fetal glucose → ↑fetal insulin (important growth factor in utero) → fatter and larger baby, ↑haemoglobin
 - Small babies: Double whammy: lack of substrate and ↑requirements (eg cold quicker)
 - If septic or otherwise sick (may also go hyperglycaemic due to cortisol and adrenaline)
- Symptoms:
 - Usually none. Can be asymptomatic at < 1 mmol/litre of glucose [would cause convulsion in adult]
 - May be jittery (but most common cause is difficult delivery)
 - Convulsions or floppy (post-ictal) – late sign
- Prevention:
 - Identify at risk babies and monitor blood glucose
 - Feeding is usually required (normal babies can go 48 hours without a feed)
 - May need IV glucose
 - Prevent hypothermia. If they're small and get cold they will become hypoglycaemic

Jaundice

- Key question is why, not by how much (although this is important too)
- Two types of bilirubin:
 - Unconjugated:
 - If ↑↑unconjugated → kernicterus: cerebral palsy, deafness, ↓IQ
 - Can die acutely (seizures, bilirubin encephalopathy)
 - If survive: deaf, athetoid cerebral palsy (snake like movements – the harder they try to move the harder it becomes), normally intelligent
 - Conjugated: water soluble, conjugated in liver by glucuronyl transferase
- Early onset (**in 1st 24 hours**):
 - Always pathological
 - Causes:
 - Haemolysis of any cause (eg Rhesus, ABO blood incompatibility, spherocytosis, G6PD deficiency etc)
 - Sepsis: respiratory distress + jaundice (not common)
 - Exam:
 - Maybe hydrops fetalis, large liver, large spleen (site of haemopoiesis in newborn)
 - Sepsis: especially breathing (indrawing and difficulty) – if in doubt then culture and stat antibiotics
 - Prevention:
 - Expect ABO if they've had it before
 - Check for Rhesus disease
- Jaundice in **1st week**:
 - Emphasis on extent of the jaundice (as well as consideration of the cause)
 - Treatment:
 - Phototherapy (visible light at the blue end of the spectrum – not UV)
 - Exchange transfusion
- **Persistent** jaundice:
 - If it doesn't go away by 10 – 14 days then revisit
 - Causes:
 - ↑Conjugated bilirubin (go green) – needs treatment

- Liver obstruction abnormalities (eg biliary atresia, secondary to liver damage from infection, toxins, etc)
- Hepatitis/liver inflammation
- Unconjugated (yellow) – needs treatment if high. Eg Breast milk jaundice – progesterone in breast milk delays maturation
- Diseases picked up on Guthrie card causing jaundice:
 - Hypothyroidism
 - Galactosaemia
 - Cystic Fibrosis
- Aside: ABO Blood Incompatibility
 - Maternal antibodies from mother with type O blood attack fetal blood cells if type A, B, or AB. Not isoimmunisation – it's an existing immune response. Doesn't get worse with subsequent pregnancies
 - Transfusion:
 - Want to transfuse type O RBCs – aren't antigenic to anyone
 - Want to transfuse type AB plasma – won't contain antibodies to either type A or B blood

Other Neonatal problems

*Infant Drug Withdrawal Syndrome **

- For first 2 weeks after delivery if mother is abusing heroin, methadone, other narcotics:
 - Jitteriness
 - Sneezing
 - Yawning
 - Poor Feeding
 - Vomiting
 - Diarrhoea
 - Weight loss
 - Seizures

*Child of Diabetic Mother **

- Maternal complications: polyhydramnios, preterm labour, still birth near term
- Fetal: ↑ malformations, macrosomic, growth retarded
- After birth: hypoglycaemia, hypocalcaemia, respiratory distress (surfactant doesn't ↑ till later in gestation), polycythaemic (venous haematocrit > 0.65, looks plethoric. May require exchange transfusion to remove RBCs)

*Transient Tachypnoea of the Newborn **

- Occurs in both term and prem babies
- ?Delayed absorption of amniotic fluid from lungs
- Risk factors: C-section, perinatal asphyxia, excessive analgesia, hypothermia
- Presentation: subcostal recession, grunting, and cyanosis all seen but not prominent
- CXR: inflated lung fields, perihilar opacities, ↑ vascular markings
- Treatment: O₂ for several days, respiratory failure uncommon. Penicillin if ?congenital pneumonia

*Meconium Aspiration **

- Hypoxia during labour → gasp → aspirate meconium (+/- vernix, meconium, blood)
- → Patchy lung collapse and over inflation (ball valve effect)
- Complications: pneumothorax and pneumomediastinum (→ angel wing appearance on CXR due to air under the thymus)
- Treatment: suction via ET tube

Heart Disease in Children

The Blue Baby

- Neonatal adaptation:
 - With first breath:
 - Alveolar oxygen tension increases
 - Pulmonary bed dilates

- Ductus arteriosus starts to constrict
- Cord clamp:
 - ↑ In LV and LA pressure
 - Functional closure of foramen ovale
- Ductus: closes at 24 – 48 hours. A murmur may be normal. Can open or close it with drugs (NSAIDS close, prostaglandins open)
- Replacement of HbF with HbA from 24 weeks (90%) to birth (70%) to 6 months (trace)

Clinical Signs of Heart Disease

- Clinical warning signs:
 - Early murmurs in a clinically well baby
 - New-born who becomes hypoxic
- Classifying:

	Cyanotic Heart Disease	Acyanotic Heart Disease	Respiratory Disease
Cyanosis	Severe	Variable	Variable
Tachypnoea	Mild	Variable	Variable
Respiratory Effort	Not major	Variable	Variable
Heart Murmur	+/-	+/-	None
When	First 1 – 7 days	First 1 – 4 weeks (effect of failure – takes longer)	Often at birth

Causes of Cyanosis

- Respiratory Causes:
 - Hypoventilation: Central apnoea from drugs, apnoea of prematurity, sepsis, metabolic (eg hypoglycaemia), seizures
 - Mechanical interference with lung function: airway obstruction, abdominal distension, pneumothorax, thoracic and sternal deformities, etc
 - V-Q mismatch with lung disease:
 - Infection (Gp B Strep, G – ive): pneumonia on X-ray hard to distinguish from wet-lung of early respiratory distress. Have high index of suspicion, low threshold for antibiotics
 - Respiratory Distress Syndrome: X-ray appearance: Ground glass + air bronchogram ⇒ ↓surfactant. If maternal diabetes, are deficient in surfactant until later in gestation
 - Aspiration: meconium, milk, blood
 - Pulmonary oedema, hydrops fetalis (⇒ in heart failure before delivery. Used to be due to Rhesus negative disease prior to Anti-D treatment, now numerous other causes)
 - Lung haemorrhage: complication in premature
 - Primary lung disease
- Cardiac causes of cyanosis:
 - R to L shunt: Cyanotic heart disease or pulmonary hypertension
 - L to R shunt *and* Heart failure
- Differentiating Heart and Lung Disease:
 - History and exam:
 - When did it start
 - Relationship of cyanosis to birth. If heart, pink to start with then go blue as ductus closes (blood gets to lungs via reverse flow through ductus if right heart not functioning well)
 - Check respiration:
 - If apnoea ⇒ heart. If heart problems, won't work so hard at breathing
 - Respiratory distress and ↑ effort ⇒ airway or lung problem
 - By investigations:
 - CXR (heart size, lung fields)
 - ABG/O2 saturation monitoring. If lung disease, may have ↑CO2
 - Hyperoxia test: put in 100% O2 – if heart disease then won't change PO2 as gas transfer is not the problem
 - Echocardiography
- Also consider sepsis and anaemia

Congenital Heart Disease

Summary

- Congenital
 - Acyanotic: Ventricular septal defect (VSD), Atrial septal defect (ASD), Atrioventricular Septal Defect (AVSD) and Patent ductus (PDA)
 - Cyanotic:
 - Decreased Pulmonary Flow (\rightarrow dark lungs on X-ray):
 - Critical pulmonary atresia/stenosis, critical aortic stenosis (if not critical the acyanotic)
 - Tricuspid atresia
 - Fallot's Tetralogy (commonest congenital cyanotic problem, presents about 3 months of age, no murmur)
 - Increased pulmonary flow:
 - Transposition of the great arteries (TGA): Fine till birth, goes blue as ductus closes
 - Total anomalous pulmonary venous drainage (TAPVD): very rare
 - Other: Coarctation
- Acquired: Rheumatic fever
- Arrhythmia: Long QT, SVT, Pre-excitation, VT
- If chronic leads to developmental delay and clubbing
- Associated with:
 - Chromosome disorders: Trisomy 21 (40% have cardiac lesion – mainly AVSD), 18, 13 and Turners (coarctation)
 - Numerous syndromes

Aetiology

- Genetic causes:
 - 6 – 8/1000 live, full term births (higher in premature and still born). Second most common congenital malformation after the brain
 - Chromosomal eg Down Syndrome
 - Single gene eg Marfan's (prolapsing mitral valve)
- Environmental:
 - Infection (eg Rubella)
 - Maternal (eg Diabetes)
 - Substance abuse (eg alcohol)
 - Drugs (eg phenytoin, thalidamide)
- Usually leads to an abnormality in tissue migration

Incidence (Pathology not Paediatrics' numbers!)

Acyanotic (L-R Shunt)	Ventricular Septal Defect	25 – 30%
	Atrial Septal Defect	12 – 20%
	Patent Ductus	10 – 15%
Cyanotic (R-L Shunt)	Tetralogy of Fallot	8 – 15%
	Transposition of Great Vessels	8 – 10%
No Shunt	Coarctation of the Aorta	5 – 7 %
	Pulmonary Stenosis	5 – 7%
	Aortic Stenosis	4 – 5 %

Ventricular Septal Defect

- Epidemiology: 12/10,000
- Types are muscular, perimembranous and outlet (affects aortic valve)
- 90% involve membranous septum which grows down to meet muscular wall
- Clinical:
 - Wide range: from asymptomatic through life to fulminant heart failure in infancy
 - Signs:
 - Pansystolic murmur (often with thrill)
 - Features of heart failure
 - Features of pulmonary hypertension if large: \uparrow JVP, sternal heave (\uparrow RH work), loud P2
- Investigations:
 - ECG: LV hypertrophy (due to volume loading)

- CXR: ↑ heart size, ↑ vascular markings in lungs
- Echo: size and location of defect
- Management: Treat only if large: surgical repair
- Prognosis dependent on size of defect:
 - Small defects often close over spontaneously. Remaining ones at risk of infective endocarditis. Prophylaxis if dental work.
 - Large defects → Eisenmenger's syndrome (see below, pulmonary hypertension, shunt reversal and cyanosis)

Atrial Septal Defect (ASD)

- Epidemiology: 6 – 8/10,000 live full term births. F:M = 2:1. Higher in stillborn and premature births
- Aetiology unknown in > 90% of cases
- Pathogenesis:
 - Septum primum closes foramen primum at week 5. Failure to form completely results in a low ASD adjoining AV valve
 - Septum secundum closes over foramen secundum at week 4 – flap forms a one-way valve. If it fails to reach far enough leads to fossa ovalis ASDs. Common in trisomy 21
 - Defects in primitive sinus venosus lead to ASD near vena cava ostia
- Clinical:
 - A L → R shunt increases pulmonary flow but if < 1 cm may be asymptomatic through life
 - Larger defects → arrhythmias and/or murmur in 3rd decade. Evaluate for corrective surgery to prevent pulmonary hypertension, heart failure or arrhythmia
 - Chronic pulmonary flow 2 – 4 times normal → pulmonary hypertension with R → L shunt and heart failure in less than 10% of cases
 - Signs:
 - May have evidence of RH overload: ↑JVP, sternal heave, loud P2
 - Ejection systolic murmur in pulmonary region (flow murmur due to ↑flow, not due to defect). This is not specific – many children have it, especially when ill ⇒ P2 important in differentiating benign from ASD
 - Fixed splitting of S2
- Investigations:
 - ECG: RV hypertrophy and Right axis deviation (due to RV volume loading)
 - CXR: ↑ heart size, prominent pulmonary artery with ↑ vascular markings
 - Echo to confirm diagnosis
- Management: Surgical or percutaneous closure by age 5 (unless small and spontaneous closure)

Patent Ductus Arteriosus

- Aetiology: Occurs as an isolated lesion or in combination with other abnormalities (eg Tetralogy of Fallot). Association with Rubella. 90% isolated defects. Incidence 1 in 2000
- Pathogenesis:
 - Connects aorta to left pulmonary artery (acts as R → L shunt in foetus).
 - ↑Oxygenation at birth → ↓PGs (lungs metabolise them) → muscular contraction → functional closure at 2 days, anatomic closure at 2 – 3 months. Forms ligamentum arteriosum.
 - If hypoxia at birth then it can remain patent. A patent ductus allows up to 75% of LV output to flow from the aorta to the pulmonary artery (ie becomes a L → R shunt)
 - If persistent then → pulmonary hypertension → becomes a R → L shunt (Eisenmenger's Syndrome – see below), deoxygenated blood flows more to legs than arms → clubbing in toes not fingers
- In term infants: Delayed closure due to ↓PaO₂: pulmonary disease (eg meconium aspiration), pulmonary hypertension, high altitude
- In preterm:
 - ↑Incidence with ↓ birth weight
 - ↓ Sensitivity to PaO₂ and ↑ sensitivity to PGE2
 - Haemodynamic effect of hypoperfusion and hypotension: associated with intraventricular haemorrhage and necrotising enterocolitis
- Clinical:
 - Murmur at left sternal edge, 2nd or 3rd intercostal space: systolic only. Silent if high pulmonary artery pressures (can be heard in first few hours in many infants)
 - Active precordium with bounding pulses and ↑ pulse pressure (collapsing pulse)

- Hepatomegaly
- LV failure: apnoea, bradycardia
- → LV hypertrophy, RV hypertrophy secondary to pulmonary hypertension if persistent
- Investigations:
 - ECG usually normal. LV and/or RV hypertrophy if large and persistent
 - CXR: cardiomegaly and pulmonary plethora
 - Echo: diagnostic
- Management:
 - Requires closing:
 - NSAIDs (anti-PG) → promote closure
 - Surgical or device closure
 - Small risk of endocarditis if closed

Persistent Pulmonary Hypertension

- Failure of pulmonary capillary bed to dilate sufficiently after birth
- Return to fetal circulation (ie R→L shunt): ↓ pulmonary flow
- Causes:
 - Aspiration, eg meconium
 - Hypoxia: asphyxia
 - Infection: Group B strep
 - Hyaline membrane disease
 - Lung hypoplasia

Coarctation of the Aorta

- Preductal or infantile form:
 - Narrowing of the arch of the aorta between the left subclavian artery and ductus arteriosus. Association with patent ductus and ASD (?due to low flow in this area after birth) and with bicuspid aortic valves. Associated with Turner's Syndrome. Severe consequences: LH failure, cyanosis in lower half of body
 - Variety of presentations:
 - Heart failure in infancy (LV hypertrophy due to pumping against an ↑ load)
 - Hypertension in child/young adult
 - Asymptomatic murmur
 - Exam:
 - ↓Femoral pulses, radio-femoral delay
 - Upper limb hypertension
 - Systolic murmur heard anteriorly and posteriorly (in back). Continuous murmur if severe
 - Investigations:
 - ECG shows evidence of LV hypertrophy
 - CXR:
 - Rib notching due to collaterals (> 5 years of age)
 - Abnormal aortic arch contour: look for faint post stenotic dilatation below cardiac knuckle
 - Echo: shows lesion – harder to see descending aorta
 - Cardiac catheter: assess haemodynamics
 - Treatment: surgery, balloon angioplasty and ongoing management (hypertension, risk of dissection, etc)
- Post ductal or adult form: Less severe narrowing with possible post-stenotic aneurysm due to turbulence. Ductus is closed. May be asymptomatic. Possible LV hypertrophy. Left intercostal artery provides collateral flow. (NB Proximal aneurysms occur in Syphilis, Coarctation and Marfan's)
- Left and right pulses may be different (left bounding)

Tetralogy of Fallot

- Malformation during closure of the interventricular septum leads to:
 - Transposition/over-riding aorta
 - High VSD
 - Pulmonary valve stenosis/atresia
 - Right ventricular hypertrophy (giving a boot shaped heart – diagnose on X-ray)
- Survival requires a patent ductus

- Clinical: RH failure, commonly endocarditis with subsequent brain abscess. Present several months after birth with episodic blueness. Death likely at puberty if not corrected

Transposition of the Great Arteries (TGA)

- Aortic and pulmonary arteries transposed → 2 separate circuits
- Requires a patent ductus +/- VSD
- OK until birth. Go blue as ductus closes

Pulmonary Valve Stenosis

- Similar effect to pulmonary atresia
- → ↓ Right heart development. Blood has always got to LA via foramen ovale, rather than through lungs

Other

- Truncus arteriosus: congenital malformation in which the pulmonary artery and aorta have failed to separate from their common precursor truncus

Arrhythmias in Children

- Relatively uncommon in paediatric population
- Often not associated with other heart disease (cf adults, associated with structural disease)
- Clinical
 - Asymptomatic or palpitations
 - If prolonged may → growth retardation, heart failure, arrest, etc
- Classification:
 - Bradycardias:
 - AV Block:
 - 1st and 2nd degree: normal variant
 - 3rd degree: Associated with AVSD, post-surgical, Rheumatic fever, myocarditis, maternal mumps, etc. Acute treatment: Isoprenaline/Atropine → ↑HR. Long term: pacemaker.
 - Sinus node dysfunction
 - Tachycardias:
 - Supra-ventricular tachycardia (SVT): due to re-entrant pathway associated with A-V node.
 - Generally paroxysmal. Regular rhythm. Normal QRS duration. 1:1 A-V conduction.
 - Management: Terminate tachycardia: vagal manoeuvres (ice on face, valsalva – breathing against closed glottis, carotid massage), IV adenosine (A-V node blocker), β-blockers, DC cardioversion. Prevent recurrences with β-blockers or ablation of re-entry pathway
 - Ventricular Tachycardias: rare in children. Cardiovert.
 - Pre-excitation Syndromes: Wolfe-Parkinson White. Accessory pathway from atria to ventricle → short PR interval, wide QRS and delta wave. Risk of cardiac arrest and sudden death. Treatment: ablation
 - Long QT syndrome: due to congenital (K⁺ channel abnormality) or acquired (drugs, hypocalcaemia). Susceptible to arrest, torsades and bradycardias. Consider in unexplained syncope or convulsions. Treatment: cardiovert if arrhythmia, β-blockers or pacemaker to prevent

Complications of Congenital Heart Disease

Heart disease with failure

- Definition: inability of myocardium to meet metabolic needs of the body
- Causes:
 - Congenital Heart disease:
 - Lesions with left to right shunt: Large VSD (→ ↑blood to pump → overloaded heart), AV canal defect, Patent ductus
 - Left outflow obstruction: Hypoplastic left heart, Coarctation of the aorta, aortic stenosis
 - Arrhythmia: usually SVT
 - Cardiomyopathy: Usually ischaemic, due to birth asphyxia
- Incidence by age:
 - Infants: congenital heart lesions, rarely arrhythmias (eg SVT)
 - > 1 year: cardiomyopathy, right heart disease, dysrhythmias

- Symptoms of heart failure: ↑respiratory effort, sweating, poor feeding (no energy to suck), failure to thrive (hypermetabolic state and poor feeding due to breathlessness)
- Signs of heart failure: Tachycardia (↑160 in infants), tachypnoea (intercostal indrawing, wheeze), gallop rhythm, hepatomegaly
- Features *not* found in children:
 - ↑JVP
 - Peripheral oedema
 - Crepitations in lung fields
- Key differential to acute onset is sepsis
- Treatment:
 - Rest
 - Diuretics
 - Digoxin
 - O₂
 - Adequate calories: fortified feeds
 - Treatment of underlying cause (arrhythmias, infections, anaemia, etc)

Eisenmenger's Syndrome (Pulmonary Hypertension)

- Sequalae of large L → R shunt with untreated VSD, PDA or ASD. Rare – as there usually corrected
- Usually present in 3rd to 4th decade
- ↑ Pulmonary flow → oversupply of blood → pulmonary capillary hypertrophy → ↑resistance → pulmonary hypertension →:
 - Reversal of shunt (R → L) → development of cyanosis
 - RH hypertrophy and failure
- Also abnormal flow → mural thrombosis → endocarditis (as in most congenital defects)
- Clinical:
 - Signs of pulmonary hypertension: RV heave, loud P2, hepatomegaly
 - Little or no murmur
 - Cyanosis, clubbing
- Prognosis:
 - Arrhythmias and sudden cardiac death
 - ↑Hb due to cyanosis (polycythaemia) → ↑viscosity → clotting problems
 - ↑Risk of systemic emboli (lungs don't act as a filter for emboli)
 - Haemoptysis due to pulmonary infarct/haemorrhage
- Treatment: Supportive or heart-lung transplant

Rheumatic Fever

- Incidence:
 - Incidence has declined over last 50 years, from death rate of about 20/100,000 to 6/100,000
 - 1 per 1000 people in NZ (highest rate in western world).
 - Annual incidence in NZ per 100,000: European 0.1 – 0.3, Maori 6.1 – 11.3 (ie 50 – 100 times), Pacific Island 13.3 – 24.3 (ie 100-200 times). Pockets in Porirua, South Auckland
 - Acute attacks occur mainly between 5 – 15 years of age. Peak 10 – 11 years.
- Aetiology:
 - Incidence following strep throat is 0.3 % (sore throat for 1 week) to 3% (sore throat for 3 weeks)
 - ?Some at ↑ risk due to longer carriage of strep → ↑ antibody response
- Pathogenesis: Group A β-haemolytic streptococci infection (eg Streptococcus Pyogenes) → cross reactive antibodies – substances in myocardium similar to strep antigens to significant inflammatory reaction in cardiac muscle → acute rheumatic fever 1 – 5 weeks following infection (average 19 day latent period).
- Clinical features:
 - Carditis:
 - Endo +/- myo +/- peri
 - Usually mild in first attack
 - New left sided diastolic murmur: mitral and/or aortic regurgitation
 - Tachycardia
 - PR prolongation (may be buried in T wave)
 - Cardiomegaly: due to valve dysfunction (→ dilation) or myocarditis

- Arthritis:
 - Migratory polyarthritis – as one joint starts to recover another flares
 - Usually large joints. Can be red and swollen
 - Dramatic response to aspirin
 - Never permanent joint damage
- Chorea (St Vitus Dance):
 - Sudden or gradual onset. Acute onset chorea in a child only occurs in RF
 - Usually generalised, although can be focal
 - Deterioration at school, eg writing
 - Stops during sleep
 - Increased by anxiety/stress
 - Rare symptom. Always resolves, after 2 – 3 weeks
- Erythema Marginatum:
 - = Red rash around edge, centre normalises as it expands
 - Evanescence (comes and goes quickly)
 - Not itchy, blanches with pressure, mainly on trunk and proximal limbs
- Subcutaneous nodules: small, painless, over bony prominences, RARE
- Investigations:
 - Throat swab: +ive for strep in 15%
 - ESR usually > 100 (not if chorea or CHF)
 - CXR: looking for cardiomegaly
 - ECG: prolonged PR in 14%
 - Echocardiogram
 - Streptococcal titres
- Diagnosis:
 - Acute Phase: Jone's criteria: evidence of strep throat (\uparrow serum titres) plus 2 major or 1 major/2 minor:
 - Major criteria: carditis, migratory polyarthritis of major joints (75%), erythema marginatum (non pruritic, non painful), subcutaneous nodules, and chorea (later)
 - Minor criteria: fever, arthralgia, \uparrow acute phase proteins, c-reactive protein, ESR, \uparrow PR interval
 - Also watch out for murmurs, arrhythmias (from focal fibrosis)
 - Very difficult to diagnose. Always consider as differential in pyrexia of unknown origin
 - Chronic Phase: recurring attacks magnify cardiac injury. Mitral and/or aortic stenosis progresses to congestive heart failure. Recurrent attacks make it worse → ?long term prophylaxis
- Treatment:
 - Eradicate streptococcus
 - Aspirin: 75 mg/kg/day (\downarrow inflammation)
 - Bed rest if cardiomegaly or CHF, others should avoid rigorous exercise
 - Steroids for acute treatment – but doesn't affect long term prognosis
 - Diazepam for chorea
- Course:
 - Acute phase lasts 6 – 8 weeks, monitored by ESR
 - Dental check
 - Ongoing management:
 - Will get it again if they get another strep infection, and more severe
 - Penicillin prophylaxis: 4 weekly IM benzathine penicillin until 18 if no cardiac damage (for life if damaged).
 - Regular dental care. Prophylaxis for deep dental work (erythromycin or clindamycin – won't have any penicillin sensitive organisms on board)
 - Valves can recover
- Macroscopic appearance:
 - Acute (exudative and proliferative) phase: Pancarditis grossly visible in valves and pericardium. Valve leaflets have evenly spaced small 1 – 2 mm sterile/inflammatory (not infective) 'verrucae' – small vegetations resulting from deposition of fibrin along edges of valve. Verrucae resolve but Aschoff bodies (areas of necrosis surrounded by macrophages) organise and fibrose. Mitral valve always involved. Pericardium show non-specific serofibrinous (bread and butter) pericarditis similar to uraemia or acute MI

- Chronic (healed) phase: Heals with organised fibrosis → deformed valves (50% mitral, 50% mitral and aortic) and/or shortening/thickening/fusion of chordae tendinae. Subendocardial fibrosis → fibrous plaque (McCallum's patch). Characteristic “fish mouth” stenosis → atrial hypertrophy and LV atrophy. Aortic stenosis → LV hypertrophy. May lead to murmurs or arrhythmias
- Microscopic appearance:
 - Exudative phase: fibrinoid necrosis with neutrophils, lymphocytes, plasma cells and macrophages
 - Proliferative phase: Aschoff body in the myocardium is pathognomonic. Consists of central fibrinoid exudate/necrosis with aggregates of large mononuclear or multinuclear cells (Aschoff giant cells), fibroblasts, plasma cells, lymphocytes and oedema. Aschoff bodies may also be seen in perivascular spaces, joint capsules, tendons, subcutaneous tissues
- Susceptible to later valvular infection
- Treatment: Possible surgical replacement of deformed valves

Respiratory Illness

- See Allergic Rhinitis, page 63

Symptoms

- Differential of dyspnoea
 - Heart failure
 - Cerebral hypoxia
 - Metabolic acidosis
 - Respiratory Causes
- Differential of Stridor:
 - Retropharyngeal abscess: lymph nodes in midline behind pharynx, usually under 4 years, mainly strep, maybe staph aureus. Acute toxicity, hyper-extended, quiet stridor, CT diagnostic
 - Croup
 - Epiglottitis
 - Foreign Body
 - Angio-oedema
 - Peritonsillar abscess
 - Laryngomalacia: noisy breathing due to floppy larynx from birth, especially inspiratory, crying or exertion
 - Tracheomalacia: soft tracheal cartilages: Brassy cough (honking). May get severe obstruction
 - Adenoid and tonsillar hypertrophy: reaches peak at 8 – 10 years, but relatively largest at 5 – 6. Snoring and obstructive sleep apnoea. Acutely enlarged → stridor (eg in EBV – treat with steroids)

Chest Radiology

- Initially:
 - Name, date, and view
 - Orientation: L & R
 - Check exposure: lung fields and intervertebral discs
 - Centering: check rib length on each side for rotation (clavicles unreliable)
 - Lung field size:
 - 5 – 7 anterior ribs to the midline of the Right diaphragm
 - 7 – 9 posterior ribs to the spine
 - If too many, then hyperinflated: asthma, CF
 - If too few, then inspiratory film: hard to interpret
- Middle right lobe is against RH border – consolidation there will obscure border. No other consolidation will
- Staph pneumonia → pneumatocele (air filled cysts). Generally resolve
- Pneumo-mediastinum → ‘angel wing’ appearance as air lifts up thymus
- Chylothorax: lymph surrounding lung in the newborn → ?thoracic duct dysfunction
- Trachea: in an infant is floppy, so in an expiratory film can have a kink
- Lateral CXR:
 - Vertebrae should get blacker as go down
 - Retrosternal clear space: in infant whiter due to thymus
- Thymus on AP CXR:

- Lots of variation – can look like large heart
- Thymic notch: lower right or left edge as it abuts the heart
- Thymic wave sign: contour down the side of the thymus
- Thymic sail sign: sail-like shape sticking into the lung fields
- Respiratory Distress Syndrome:
 - = Alveolar collapse (not bronchi)
 - Xray: diffuse opacity, air bronchograms and small lung volume
 - Severity assessed by blurring of heart borders and diaphragm
 - Group B Strep infections in full term babies can look a bit like it
- Transient Tachypnoea of the Newborn:
 - Xray: Retained lung fluid, lung volumes normal to large, and pleural effusions
 - Mild → recover
- Meconium Aspiration:
 - Xray: Diffuse, coarse lung field opacity (fluffy), hyperinflated (airway pathology not air space pathology → plugging and ball/valve effect)
 - Can get pneumothorax, pleural effusions due to the work of breathing
 - Mainly in term babies – they have the grunt to suck it down. Also, pre-term babies less likely to pass meconium when stressed

Respiratory Tract Infections in Children

- Reference: Mainly from Prof Grimwood's extensive infectious diseases handout
- Epidemiology:
 - Common: During the first 3 years of life, a child may have up to 6 episodes of otitis media, 2 episodes of gastro-enteritis and 6 respiratory infections per year. 10 – 15% have 12 colds per year.
 - Other risk factors:
 - Breast feeding is protective
 - Passive smoking
 - Exposure to infection: older siblings, day care, etc
 - Socio-economic status (multifactorial)
 - 95% of respiratory infections involve the upper respiratory tract and 90% are viral
 - But antibiotics prescribed in 70% of cases. Leads to:
 - Unnecessary adverse effects: rashes, diarrhoea, thrush, plus more serious ADRs
 - ↑Cost
 - Antibiotic resistance → major increases in cost. Especially *S pneumoniae* and *S. aureus*
 - Reduce unnecessary prescribing by developing guidelines, practitioner education, public relations and ↓OTC antibiotic sales (eg mupirocin)
- Pathogenesis: 60% due to rhinoviruses and coronaviruses, then RSV, parainfluenza viruses, influenza and adenovirus

Common cold

- Starts with nasal congestion, throat irritation → sneezing, watery nasal discharge
- Low grade fever, malaise, cough, headache
- After 1 – 3 days nasal discharge becomes thicker and mucopurulent. This is part of the natural history of URTI and does not indicate a bacterial super-infection
- Generally improved by day 10, although cough (in 30%) and nasal discharge (in 40%) may persist for > 2 weeks
- Numerous RCTs have consistently failed to show that antibiotics alter the course of the common cold

Acute Otitis Media

- = Infection of the middle ear cleft
- Presentation:
 - Eardrum opaque (not semitransparent), red, normal landmarks lost, bulging. But if kid is screaming, ear will be red regardless
 - Otolgia, otorrhoea, hearing loss
 - Systemic signs: fever, irritability
 - If it ruptures, child will be instantly better (but parents will panic!). Acutely ruptured eardrum will heal in 24 hours
- Pathogens:
 - *S pneumoniae* (30 – 50%)

- Non-typeable strains of H influenzae (20 – 30%)
- M Catarrhalis (10 – 20%)
- Viral (10 – 20%) especially RSV
- Mixed bacterial/viral infections account for 50% of antibiotic failures
- Treatment:
 - Without treatment, 70 – 90% of infections resolve spontaneously
 - Those least likely to respond are:
 - Aged < 2 years
 - Those with constitutional disturbance (eg > 39 C)
 - Where S pneumoniae is the pathogen
- Antibiotics:
 - Should be directed against S pneumoniae: it is the most common pathogen, the least likely to resolve spontaneously, and the most commonly associated with mastoiditis. Amoxycillin for 7 – 10 days (?5 days just as good) is the treatment of choice, even when there are non-susceptible S pneumoniae isolates. Good penetration of middle ear. Erythromycin/cotrimoxazole if allergic. Main reason for antibiotics is to prevent rare complications
 - For the 90 – 95% of otitis media that responds to antibiotics, 90% are due to spontaneous resolution
 - If < 2 years, constitutional disturbance and persistent symptoms > 48 hours:
 - Amoxycillin 15 – 30 mg/kg TID for 10 days (ie high dose).
 - If no improvement after 48 – 72 hours try Augmentin (cover H influenzae and Moraxella)
 - Main aim is to reduce the very small chance of suppurative complications
 - Treatment for Acute Otitis Media in children (NZ Guideline for Acute Otitis Media):
 - Main benefit from antibiotics is less pain on the 2nd or 3rd day in 1 in 17 kids, and failure to spread to other side in 1 in 17. No effect on pain on first day, prevention of recurrence or build up of middle ear fluid
 - Side effects of skin rash, vomiting or diarrhoea are as common as benefits
 - Recommendation: use Paracetamol, return to doctor if symptoms persist beyond 48 hours, and have ears checked in a month for persisting fluid (common in first several weeks) – this occurs in about 1 in 10
 - Oral cephalosporins and 2nd generation macrolides don't penetrate the middle ear and/or have poor activity against S pneumoniae
- Complications:
 - Mastoiditis in 0.1%. Incidence is not increased by delayed treatment
 - Little evidence to suggest that untreated otitis media causes mastoiditis
 - Very rare: petrositis, labyrinthitis, facial palsy, subdural/epidural/brain abscess

Recurrent Acute Otitis Media

- Risk factors for recurrent acute otitis media: childcare centres, passive smoking, family history, reflux
- Management:
 - Ensure correct diagnosis
 - Reassure: spontaneous improvement in many after age 2 – 3 years and during summer
 - Limit passive smoking, discourage pacifier use
 - Encourage breast feeding in infancy
 - Antibiotic prophylaxis generally ineffective
 - Avoid unproven therapies: antihistamines, decongestants, chiropractic, homeopathy and naturopathy
- Refer to paediatrician/ENT surgeon if febrile seizures, antibiotic intolerance, hearing loss/speech problems, underlying facio-cranial abnormalities
- In the future, conjugate pneumococcal vaccines are likely to play an important role

Chronic Otitis Media with Effusion

- = Presence of sterile *or* infected fluid in middle ear
- Chronic OME (=Glue Ear) if > 3 months. If it hasn't cleared by then, less likely to clear spontaneously.
- Common up to age 5 or 6
- Symptoms:
 - Incidental finding in asymptomatic child

- Hearing loss and its effects: speech delay, slurred speech, failing at school, irritable, poor balance, falling over. But delayed language and cognitive problems related more to genetic and SES than previous otitis media
- Pathogenesis: eustachian tube dysfunction (not just blockage)
- Sequela of otitis media: Middle ear effusion:
 - In 70% after 2 weeks
 - In 50% after 1 month
 - In 20% at 2 months
 - In 5 – 10% after 3 months
 - Associated with mild hearing loss.
- Treatment:
 - Effusion common after an ear infection. Watch and wait
 - If bubbles behind ear drum then it's resolving itself
 - Drugs: antibiotics and decongestants not very effective
 - If persisting > 3 – 6 months:
 - Test hearing
 - Limit passive smoke exposure
 - Treat underlying allergic rhinitis/adenoinal enlargement with intra-nasal steroids
 - Refer after 3 – 6 months if hearing loss and:
 - Failure to respond to antibiotics
 - Recurrent acute otitis media
 - Persistent otalgia
 - Retraction pockets
 - Expressive/receptive language delay
 - Underlying cranio-facial abnormalities (eg Down syndrome)
 - ENTs say grommets are the treatment of choice: Aerate middle air ($\rightarrow \downarrow \text{CO}_2 \rightarrow \downarrow \text{squamous metaplasia} \rightarrow \downarrow \text{goblet cells} \rightarrow \downarrow \text{effusion}$). Extrude over 18 months – 2 years. Take out if still there 5 yrs later. May take out adenoids at same time $\rightarrow \uparrow \text{eustachian tube function}$ (Paediatricians say adenoidectomy is treatment of choice).
 - Precautions with grommets:
 - Plug ears when washing hair and bathing
 - Can swim in clean fresh water but no diving below the surface
- Chronic Suppurative Otitis Media – with hole in drum. Treatment: get rid of infection then surgical repair

Pharyngitis

- See Acute Pharyngitis, page 63
- Almost 100% given broad-spectrum antibiotics. Inappropriate in 90% of cases
- Pathogens:
 - Viruses: Adenovirus, also rhinovirus, coronaviruses, RSV, Parainfluenza virus, influenza, enteroviruses, EBV
 - Bacteria: S Pyogenes (GABHS = Group A Beta-Haemolytic Strep) in about 20 – 30% of cases, predominantly in those over 4 years
- Differentiating (at best 70% predictive accuracy):
 - Exudative tonsillitis: Adenovirus, GABHS, EBV
 - > 4 years, enlarged tender anterior cervical lymph nodes and diffusely inflamed pharyngeal structures (+ exudates) suggests S Pyogenes
 - Diffuse, sandpaper-like red rash, accentuated in skin creases (Pastia lines) suggest Scarlet Fever. See Streptococcus Pyogenes (Group A, β Haemolytic), page 500
 - Nasal discharge, cough, hoarseness, conjunctivitis or diarrhoea +/- fever +/- tonsillar exudates suggests virus
 - Throat swabs: usually identify organism, but 10 – 50% are carriers
- Treatment:
 - Aim: Prevent acute rheumatic fever, suppurative complications (peri- or para tonsillar abscess) and hasten recovery
 - But
 - Only benzathine penicillin has been shown to reduce RF – and this was in military personnel
 - No convincing data which shows antibiotics reduce the risk of rare suppurative complications

- Antibiotics reduce symptoms by 8 hours only
- Reinforces the notion that antibiotics are effective and increases the likelihood of their future use for trivial illnesses
- If high risk for RF (eg Maori, PI, > 4 years of age) take swabs or treat empirically. However, prescribing penicillin for sore throat hasn't altered the rates of RF, and many children with RF haven't consulted their doctor
- S Pyogenes: penicillin, 500 – 1000 mg BID for 10 days (Allergy: erythromycin)

Acute Sinusitis

- Uncommon. Bacterial sinusitis complicates 0.5 – 5% of viral upper respiratory tract infections
- With most colds, nasal discharge and obstruction are improving after 2 weeks. Children with acute sinusitis will not be improving
- A minority present with high and persistent fever, periorbital swelling, facial and dental pain
- Imaging:
 - Plain x-rays don't differentiate well between common cold and sinusitis
 - CT more useful. Air-fluid levels, opacification, mucosal thickening > 4 mm
- Maxillary and ethmoid sinuses present at birth (although small). Frontal and sphenoid sinuses begin at 4 – 6 years of age
- Pathogens: S pneumoniae (30 – 70%), H influenzae (20%), M Catarrhalis (20%), virus alone (10%)
- Treatment:
 - High spontaneous cure (60% by 10 days vs 85% with amoxycillin)
 - Treat for S Pneumoniae in children with persisting symptoms which are not improving
 - Amoxycillin 15 – 30 mg/kg TID for 5 days. Higher limit if < 2 years, attend child-care, or have received antibiotics in the last month in areas with > 10% penicillin resistance
 - Consider Augmentin, co-trimoxazole, cefuroxime or ceftriaxone if no improvement after 48 – 72 hours

Bronchitis

- Inflammation in bronchial mucosa → productive cough
- Most cases are from viruses (eg RSV)
- Numerous studies have not found any evidence to support antibiotic treatment (but they're usually prescribed....)
- Production, colour or culture or sputum does NOT predict aetiology
- Consider treatment if:
 - Prolonged cough in older child: ?M pneumoniae → erythromycin
 - Pertussis and cough < 4 weeks: erythromycin (or co-trimoxazole) reduces infectivity
 - Cystic fibrosis/other chronic lung disease: tailored antibiotics
 - Prolonged cough (> 8 – 12 weeks and not from URTI): investigate for asthma, Tb, pertussis, CF, foreign body, Subacute-sinusitis, psychogenic cough

Croup

- = Laryngotracheobronchitis
- Pathogens: Usually viral: Parainfluenza 1 and 2 are the most common. Measles and influenza are the most severe. Don't give antibiotics
- Presentation:
 - Child < 5 years
 - Coryza and fever over 1 – 2 days
 - Then characteristic harsh "barking" cough, hoarseness +/- signs of upper airway obstruction (stridor, respiratory distress), *inspiratory stridor*
 - Worse at night, and peak on 2nd or 3rd night. Varies hour to hour (ie don't send them home just yet...)
 - Lasts 3 – 4 days then changes to sound productive. May last for another 2 weeks
- Differential:
 - Epiglottitis: Absent/minimal cough, low-pitched expiratory *snore*
 - Bacterial tracheitis: toxic appearing, older child, high fever, brassy cough, stridor, tender trachea
 - Laryngeal foreign body: sudden onset, unable to vocalise
 - Angioneurotic oedema: associated signs usually present
 - Retropharyngeal abscess: High fever, dysphagia, hyperextension of neck
- Assessment:

- Severe if restless, anxious, pallor, lethargy, tachycardia, tachypnoea, indrawing, cyanosis or ↓breath sounds
- Loudness of stridor is not a reliable guide to severity of obstruction
- ↑Risk of obstruction if: pre-existing upper airway narrowing (eg sub-glottic stenosis) or Down Syndrome
- Management:
 - Avoid distressing the child, settle them on parent's lap
 - Blood tests, pulse oximetry, O₂ masks and nebulisers rarely needed
 - Mild:
 - Not distressed, no stridor at rest
 - No treatment, management at home, return if signs of ↑obstruction, lots of comfort
 - Paracetamol
 - Moderate:
 - Frequent barking cough, distressed, persistent inspiratory stridor, tracheal tug or sternal retraction at rest, but no signs of hypoxia
 - Observe or admit
 - Steroids (Dexamethasone or betamethasone 0.6 mg/kg orally or im, prednisolone 1 mg/kg orally. May be repeated 12 – 24 hours later (but consider alternative diagnoses first)
 - Disturb child as little as possible
 - Severe:
 - Signs of obstruction, hypoxia (restless, irritable, anxious, cyanosis), ↓breath sounds
 - ?ICU admission
 - Nebulise adrenaline + Steroids (Prednisolone 1 mg/kg/day)
 - Monitor closely

Epiglottitis

- Caused by Haemophilus Influenza Type B
- Incidence ~ 20 cases pa (dropped from 160 in 1992 prior to vaccination)
- Presentation:
 - Incubation for 2 – 4 days
 - Acute, febrile illness, toxic looking child
 - Snore, mouth always open, drooling, prefers to sit upright. Soft inspiratory stridor, louder expiratory stridor
 - No cough (cf croup)
- Management:
 - Blood cultures
 - Intubate first, then give iv antibiotics (if given first, pain → panic → respiratory arrest)
 - Cefotaxime 25 – 50 mg/kg/8hr iv (max 2g) due to ↑penicillin resistance
 - Amoxycillin 50 mg/kg/4 hr iv (max 2g) if penicillin sensitive
- Other illnesses caused by H Influenzae type B:
 - Meningitis: 5% mortality, 10% with sequelae (retardation, seizures, hearing loss, etc), 20 – 30% have functional disabilities (eg learning difficulties)
 - Also pneumonia, empyema, septic arthritis, periorbital or facial cellulitis
- Vaccination:
 - Prior to immunisation was the most common cause of life threatening bacterial infection < 5 years of age.
 - Herd immunity now works well
 - Subunit vaccine is 95% effective. Few side effects (< 5% with local reactions)
 - Notifiable disease

Pertussis

- Bordetella Pertussis = Whooping Cough
- Epidemiology:
 - Highly contagious. Regular epidemics every 3 – 5 years in NZ
 - Incidence: up to 5000 cases a year (only a small proportion notified)
 - In first year of life 80% are hospitalised and 0.2% die
- Presentation:
 - Phases:
 - Incubation 2 – 3 weeks

- Coryzal phase: ~ 1 week
- Paroxysmal phase:
 - Develops into paroxysmal bouts: unprovoked cough followed by inspiratory gasp (whoop), apnoea, vomiting.
 - Thick tenacious sputum → can't clear → coughing spasm. Whoop may be absent in infant. If severe may need suction
 - In between paroxysms looks well, is afebrile and has no chest signs
 - Median length: 6 weeks. Can be up to 12 weeks
 - Infectious for 2 – 3 weeks of paroxysmal phase
- Persistent cough for 3 – 4 months (convalescent phase – bacteria cleared)
- Treatment: if < 4 weeks duration: *erythromycin*. Doesn't impact illness after paroxysmal phase is established, but will ↓ infectivity
- Admit if under 6 months and/or cyanosis or apnoea in paroxysms
- Complications:
 - Anoxic seizures in 1 – 3%
 - Encephalopathy in 0.1 – 0.3% → retardation, spasticity and seizure disorders. Rate of severe neurological complications of immunisation negligible compared with the risk of encephalitis from whooping cough
- Vaccine:
 - Whole cell vaccine effective in 60 – 90%, has higher efficacy for more severe outcomes, local reactions or fever in 50%. 1 in 1 million are associated with an encephalopathy (? No causal relationship established)
 - Acellular pertussis has higher efficacy and is better tolerated (< 10 – 15% adverse reactions) – now being introduced

Bronchiolitis

- Epidemiology
 - Classically RSV
 - Highly infectious acute viral respiratory illness in kids 2 weeks to 12 months of airways < 1 mm diameter
 - Epidemics every winter with RSV, also parainfluenza, influenza and adenoviruses
 - Major cause of URTI in kids: up to 50% of 1 year olds have had RSV infection
 - Seasonal in winter/spring
- Presentation:
 - Short incubation: 3 – 4 days
 - Contacts: older siblings will have had nothing more than a snotty nose
 - Difficulty with expiration (cf Croup – inspiratory)
 - Typical pattern: Starts as URTI - 1 day of runny nose, 1 day of cough, then wheeze. Illness/breathlessness worst on 4th day of wheeze (6th or 7th day of illness)
 - Low-grade fever, non-toxic, cough, wheezy, difficulty feeding, hyperinflated chest, diffuse fine inspiratory crackles and expiratory wheeze
 - If more severe then ↑ irritability, pallor, pulse > 160/min, respiratory rate 50 – 70/min, expiratory grunt (not stridor), head nodding, more marked retractions
 - Respiratory failure in 1 – 2%: pallor, sweating, drowsiness, ↓ respiratory effort, ↓ breath sounds, apnoea. Cyanosis is a late sign
 - Feeding a good indicator of respiratory distress (and one which parents can monitor at home)
 - Recurrence common (?hypoplastic airways and smoke exposure)
 - Usual recovery is 7 – 10 days
 - Can get repeat viral illness – in which history suggests fluctuation – getting better, then got worse again, etc
- Distribution of LRTI from RSV:
 - Bronchiolitis: 40 – 90%
 - Pneumonia: 5 – 40%
 - Tracheobronchitis: 10 – 30%
- Risk factors for severe presentation:
 - < 6 weeks old
 - Older siblings
 - Maternal smoking
 - Preterm delivery

- Underlying conditions: congenital heart disease, chronic lung disease of infancy, congenital abnormalities, immunodeficiency
- Differential:
 - Recurrent bronchiolitis, history of eczema, strong family history of atopy \Rightarrow ?asthma. Trial of nebulised salbutamol.
 - Persistent cough, failure to thrive \Rightarrow cardiac disease, cystic fibrosis, structural lung disease, aspiration, immunodeficiency
- Investigations:
 - Nasopharyngeal aspirate for culture and viral immunofluorescence
 - Bloods for culture and serology
 - Imaging: CXR shows hyperinflation, peribronchial thickening, often patchy areas of consolidation and collapse. Hyperinflation and wheeze differentiate it from pneumonia
- Treatment:
 - **Not** bronchodilators, steroids, ribavirin or antibiotics
 - Symptomatic treatment: O₂, rehydration, minimal handling
 - Can go home if they're feeding OK and don't need O₂
 - Admit if respiratory distress, difficulty feeding, or adverse social circumstances. If sending home early in the illness, arrange for review within 24 hours
 - Put on NG feeds: not hungry \rightarrow ↓distress
 - If respiratory rate > 70/min and feeding poorly then IV or NG fluid at 50 – 75% of maintenance requirements (risk of SIADH)
 - If oximetry < 92% then O₂
 - If severe, monitor blood gases, consider CPAP or ventilation (especially chronic respiratory/heart disease)
 - Maybe wheezy for 2 weeks and a cough for 4 weeks

Pneumonia

- Epidemiology: Peak incidence in first 2 years, and in Maori and PI children
- Presentation:
 - Initial prodromal coryzal symptoms for a few days
 - Fever, cough, tachypnoea, signs of consolidation
 - Young children may present with predominantly systemic features: fever, lethargy, vomiting, abdominal pain
 - Older children may have headache, pleuritic chest pain, irritating cough, maybe abdo pain if lower lobe or even signs of meningism if upper lobe
 - Severe if:
 - Toxic: lethargy or ↓arousal, circulatory compromise, abnormal respiration (eg apnoea, cyanosis)
 - Respiratory distress: pallor, restless, agitated, nasal flaring, grunting, head nodding, chest wall recession, paradoxical abdominal movement, difficulty feeding
- Signs on exam:
 - In infants: may be few signs, usually limited to a few focal crackles
 - Older children: ↓chest wall movement, ↓breath sounds, fine crackles, later dull to percussion and bronchial breath sounds
- Pathogens:
 - Viruses are the most common cause in infants and young children:
 - RSV and Parainfluenza 3 most common
 - Suggested by: infant or young child, coryzal prodrome, mild or moderate constitutional disturbance, hyperinflation and diffuse inspiratory crackles, patchy consolidation on CXR
 - Rarely, infections with influenza A, adenovirus 3, 7 or 21 can be severe leading to death or severe lung damage
 - Bacterial:
 - S pneumoniae most common bacteria
 - S aureus uncommon but severe, H influenzae uncommon
 - M pneumoniae common in school age children, insidious onset including anorexia, headache, scattered fine inspiratory crackles, bilateral
 - S pyogenes: typically follows Varicella, influenza A or measles, protracted course and often empyema

- Chlamydia: in 1st 2 months. Vertical transmission + eye infection in first 5 – 7 days. See Eye disorders in Children, page 631
- Investigations:
 - Imaging: CXR to:
 - Confirm diagnosis
 - Detect complications: pleural effusion, pyopneumothorax, lung abscess
 - Exclude other causes: congenital lung lesions, lung abscesses
 - Blood cultures before antibiotics
 - Nasopharyngeal aspirate for RSV detection
 - Serology for M pneumoniae or RSV
 - Aspiration of pleural fluid (assists diagnosis, and is therapeutic – antibiotics won't penetrate a large effusion)
- Treatment:
 - Penicillin G is the treatment of choice for uncomplicated bacterial pneumonia (unless allergy). Despite 20% of S pneumonia's showing reduced sensitivity, concentrations in the serum and lung tissue exceed the MIC by several fold. More treatment failures are associated with erythromycin and co-trimoxazole
 - Admit if any of:
 - < 2 years
 - Signs of toxicity, hypoxia, respiratory distress
 - Extensive consolidation or an effusion
 - Clinical or x-ray signs of Tb
 - Adverse social circumstances, no transport or no access to phone
 - If sent home, then review within 12 – 24 hours
 - For uncomplicated bacterial pneumonia: Penicillin G 25 – 30 mg/kg/6hr iv (max 2.4g)
 - If not afebrile within 24 hours on penicillin G, then review microbiology results, repeat CXR, consider other causes and treatments. Treatment failure: consider Viral, Mycoplasma, S aureus, resistant H influenzae
 - Supportive therapy: minimal handling, careful fluid management (max 50% of maintenance fluids if IV), O₂
 - Management of pleural effusion. Before antibiotics do diagnostic aspiration and urgent gram stain. Discuss with paediatric surgeon:
 - Thin clear fluid: aspirate as much as possible
 - Thin purulent fluid: intercostal drain
 - Thick purulent fluid: loculates so drain won't work ⇒ thoracotomy (consider flucloxacillin +/- Cefotaxime)
 - Infected effusion = Empyema = pus in pleural cavity
 - Fibrous septae will form around empyema = loculated empyema

Tb Pneumonia

- Rarely presents as acute pneumonia
- Consider if:
 - Known exposure to Tb
 - Child or family born in an endemic area
 - > 4 week history of cough, especially if fever, sweats and weight loss
 - Refractory pneumonia
 - Suggestive CXR
- Nurse in respiratory isolation:
 - Virtually all child cases are primary and non-infectious with a small burden of disease
 - But adolescents, those with extensive or cavitating disease, or infected visiting family are infectious
- Investigations:
 - FBC, ESR, electrolytes, CR and LFT
 - Mantoux test
 - Specimen collection: sputum if available. Early morning gastric aspirates better than lavage. Also consider urines, pleural biopsy and LP
- Empiric treatment: isoniazid, rifampicin, pyrazinamide
- Notify to Medical Officer of Health

Asthma in Young Children

- See also Asthma, page 77, especially for Medication and Spacer Use
- 3rd most common reason for admission (after Bronchiolitis and URTI/Otitis media).
- Much much less common in < 1 years (NB bronchiolitis causes wheezing in young). Peak in 2 – 4 years
- Peak flow very unreliable under age 7 (and most bad asthmatics diagnosed from 2 – 5) → *have to rely on history*
- History:
 - Symptoms: waking at night with cough/wheeze, after exercise, how often are attacks, had time off school/kindy as a result, how long does preventer last
 - Environmental factors: smokers, pets, damp, obvious triggers
 - Current treatment: medicines, do the family understand the difference between reliever and preventer, assess technique and compliance, is spacer accepted by child and is it washed
- 2 patterns on history:
 - Episodic (intermittent): viral URTI → cough and wheeze. No interval symptoms
 - Persistent (with exacerbations): interval symptoms (with exercise, at night), exacerbations with viral infection, interferes with everyday life
- Symptoms in a toddler:
 - Cough, often worse at night
 - May vomit with cough (NB exclude pertussis: cough → choke → vomit → OK for an hour. In asthma, cough again straight away)
 - Usually wheezy with URT infection
 - Diagnosis difficult in an infant unless recurrent, strong immediate family history or evidence of atopy
- Physical findings in a toddler:
 - Often normal chest exam
 - If severe chronic symptoms:
 - Hyperinflated chest (\uparrow AP diameter)
 - Harrison's sulcus: dip in chest wall where diaphragm attaches
 - Eczema
 - Reduced growth (if severe)
 - Stethoscope can be confusing
- Diagnosis:
 - Cough is very common in kids (8 – 10 per year). But more during the day than at night. Won't slow them down when running
 - Is it asthma, bronchitis, bronchiolitis?
 - Trial of therapy (preventative as well as relievers) and review
- Criteria for admission:
 - Pulse rate $> 1.5 * \text{normal}$
 - Respiratory rate > 70 minute
 - \uparrow Chest movements
 - Restlessness/apathy/CNS depression or cyanosis/pallor [signs of exhaustion]
- Severity assessment:

	Mild	Moderate	Severe	Critical
<i>Mental State</i>	Normal	Normal	Agitated	Confused/drowsy
<i>Accessory Muscle use</i>	Nil	Minor	Mod/markd	Maximal/exhaustion
- Treatment:
 - Avoid triggers: passive smoking, pets, house dust mite (dehumidifiers don't work), pollens, cold, exercise, damp houses, certain foods (overstated)
 - Infrequent episodic asthma:
 - Consider no therapy, avoid triggers
 - If distressed with attacks: use bronchodilators + spacer only. Start during URTI phase. No preventative
 - Frequent Episodic Asthma (only get it with a cold):
 - Intervals between attacks < 6 weeks
 - Bronchodilator as needed with URTIs
 - Prophylaxis:

- Sodium cromoglycate (Vicrom + spacer). ?Evidence of poor efficacy
 - Nedocromil (Tilade + spacer)
 - Inhaled steroids: if it makes no difference then stop
- Persistent Asthma
 - Male: female = 4:1
 - Preventative. If mild try Vicrom or Tilade. Moderate or severe use inhaled steroids (takes 2 – 3 months for maximal effect). Titrate back once controlled
 - Bronchodilators as required
 - Poor control: consider ↑dose, check inhaler device and technique, poor compliance, environmental triggers
- Other treatment options:
 - Long-acting β-agonists: salmeterol (Serevent), eformoterol (Foradil, Oxis)
 - Theophylline (Nuelin, Theodur): 3rd line, gut ache → poor compliance
 - If severe: *alternate* day oral prednisone treatment – reduced side effects (short and fat), and reasonable asthma control
- Protocol for an acute attack:
 - Salbutamol dose: up to 5 years: 6 puffs via space. Over age 5: 12 puffs via space
 - For severe add ipratropium (Atrovent)
 - For moderate and severe, give doses at 0, 20, 40 and 60 minutes and review at 75 minutes
 - Oral Steroid for all except minor attacks: 1 mg/Kg/day → ↓relapse

Differential of Wheezing in a Child

- Common:
 - Asthma
 - 'Happy wheezer':**
 - Diagnosis of exclusion
 - Usually < 12 months
 - Chronic *daytime* wheeze and no cough
 - Child undistressed and not impact (ie feeding OK, not waking)
 - Less wheeze when asleep
 - Requires no therapy
 - ?Collapsible airways
 - Can become an 'unhappy' wheezer when they get a cold, in which case treat as for bronchiolitis
 - Bronchiolitis:** See 610
- Uncommon:
 - Inhalation:** If convincing episode of inhaling a foreign body (stridor, went blue, etc) should be bronchoscopy – even if they think they brought it all back up. Signs: unilateral wheeze or stridor. May present months or years later with haemoptysis. CXR – will have hyperinflation or collapse on side of inhaled object
 - Cystic Fibrosis:** [see Cystic Fibrosis (CF), page 615]
 - If breast feed can still thrive for a month or two
 - Respiratory symptoms often present with wheeze not cough
 - Heart Failure:
 - Sweat when feeding + poor feeding/cyanosis
 - Wheezy – sounds like bronchiolitis
 - Look for enlarged liver (but beware, bronchiolitis → hyperinflation → liver lower)
 - Aspiration:**
 - If due to neurological problems, will cough and splutter when swallowing
 - Long vague history with unclear start
 - Gives acute onset of wheeze – eg OK when you put them to bed, but sudden coughing and wheezing later
 - If lying on back, most likely to aspirate into right upper lobe, but in practice they are wheezy everywhere
 - Hard to prove. Diagnosis of exclusion. Can do reflux probe to show they reflux often
 - Immune deficiency:**
 - Rare. Only consider if lots of serious illnesses

- Cilia dyskinesia: usually starts with ears (middle ear has respiratory epithelium with cilia), then lungs and sinuses. Associated with dextrocardia
- Hypogammaglobulinaemia
- Can confuse wheezing with soft **stridor**: eg laryngomalacia. Inspiratory sound
- Rare congenital causes: cysts, tumours, lobar emphysema, tracheomalacia/bronchomalacia (not properly formed → floppy)
- Smoking contributes to all the above:
 - Prenatally, maternally smoking → ↓airway size
 - Post-natal → inflammation/irritation

Cystic Fibrosis (CF)

- Autosomal recessive. 1 in 25 are carriers
- Disease of epithelial lined organs:
 - Lungs: mucus plugging → chronic inflammation → necrosis, adjacent pneumonia, bronchiectasis. Leads to chronic infection, emphysema and pseudomonas colonisation. Eventually → Cor Pulmonale
 - Pancreas: fibrosis around ducts, dilated ducts, islets cells relatively preserved. → pancreatic insufficiency
 - Gut → meconium ileus, biliary cirrhosis, recurrent RLQ pain
 - Bile ducts obstructed
 - Middle ear
 - Vas deferens → infertility
- Presentation:
 - Newborn screening (80% will turn out to be carriers, not diseased). Guthrie card for Immuno Reactive Tripsin (IRT). Tripsin leaks into blood from pancreas if pancreatic duct blocked. Sensitivity high (~95%) but not at all specific. If positive then → gene screen
 - Neonates: Meconium ileus:
 - > 90% with meconium ileus will have CF → obstruction at birth. Occurs in 15% of those with CF
 - Presentation: bilious vomiting, palpable bowel loops, distension if perforated
 - CXR: distended bowel loops with thickened walls
 - May also have associated volvulus, small bowel atresia, perforation, neonatal meconium peritonitis secondary to perforation
 - Treatment: enema + IV fluids or surgery
 - Failure to thrive
 - Sibling with CF
- Pathogenesis:
 - Abnormality of cAMP dependent chloride transport due to mutation of the CFTR protein. Less water gets out → thicker mucus ⇒ obstruction and ↓ciliary clearance
 - In 70% of the mutations, the protein is not glycosylated normally → not transported to site
- Testing:
 - Guthrie screening
 - Sweat test (lack of Cl channel → can't reabsorb NaCl from isotonic secretions → salty sweat)
 - Gene screen DF508/U on chromosome 7.
- Advantages of early diagnosis: ↑lung function, ↑nutrition, less traumatic diagnostic process
- Post-natal management:
 - Good nutrition: enzyme replacement, high calories, fat soluble vitamin supplements
 - Antibiotics for URTI
 - Grommets at 2 years
 - Multidisciplinary approach
- Possible monitoring tests:
 - CXR, lung function tests, sputum culture (esp pseudomonas lung infection – key prognostic indication)
 - FBC, electrolytes, total protein, albumin, Vit A, D, E, blood glucose
 - Faecal elastase (testing pancreatic insufficiency)
- Complications include bronchiectasis (CF is commonest cause): bronchi dilated and filled with purulent secretions. Like CF requires regular physio

Infectious Diseases

- See also:
 - Respiratory Tract Infections in Children, page 605
 - Gastroenteritis, page 644
 - Epstein Barr Virus, page 505
 - Herpes Simplex Virus (HSV), page 503
 - Varicella Zoster, page 504
 - Streptococcus, page 500
 - Bacterial Meningitis, page 495
 - Polio and Rubella in Vaccine Preventable Diseases, page 518

Fever in Children

- Most fevers caused by respiratory tract viral infection, are self-limiting, and require only symptomatic treatment.
- Kids have 6 – 8 viral infections each year → they are common
- Role of doctor:
 - Identify source of infection
 - Counsel caregivers and child
 - Manage the illness
 - Identify and refer those with potentially serious illness
- If no focus found:
 - Consider UTI, occult pneumococcal bacteraemia, meningitis
 - Consider non-infectious causes: rheumatic fever, poisoning, drug fever, more rarely leukaemia and other autoimmune diseases (eg Kawasaki's Disease)
 - On exam, pay attention to:
 - General appearance: activity, perfusion, colour
 - Vital signs: pulse, respiration, blood pressure
 - Exclude: fontanelle, neck stiffness, respiratory distress, abnormal chest signs, ears, throat, lymphadenopathy, hepatosplenomegaly, abdominal distension, bone or joint tenderness/swelling, skin rashes
 - At greater risk: neonates, immunocompromised, congenital abnormalities, toxic appearance, epidemiological ↑ risk (eg Maori)
 - WBC are unreliable for detection serious infection
 - Review within 24 hours and parent education
- Advice for parents:
 - Light clothing
 - Small, frequent drinks of water or fruit juice diluted 1:4, 5 – 7 mls/kg/hr
 - Paracetamol, 15 mg/kg/6 hourly, max of 90 mg/kg/day for 2 days
 - Return to doctor if refusing drink, pale or floppy, difficulty breathing, headache/neck stiffness/photophobia, doesn't improve in 48 hours
- Clues for predicting serious illness (even over the phone):
 - Responsiveness and activity
 - Feeding
 - Urine output
 - Breathing
 - Colour

Potentially Serious Infections

- See When is a child really sick?, page 565
- Sepsis: leads to systemic inflammatory response syndrome (SIRS). Also get it in major trauma, pancreatitis, etc. Mass release of cytokines. (Cf bacteraemia: bugs in blood but no major systemic reaction)
- Sepsis + focus (pneumonia, kidneys, joints/bones):
 - Neonate: Gp B Strep (S agalactiae), E Coli, S aureus
 - Infant/older child: S Pneumoniae, N Meningitidis, S aureus (complication of skin infections), S pyogenes, [HIB]
- Meningitis: infection of CSF via choroid plexus
 - See Bacterial Meningitis, page 495

- Neonate: Group B Strep, E Coli, Listeria

Common Paediatric Viruses

- Reference: Prof Grimwood's Paediatric Infectious Diseases Handout (all 94 pages of it!)

Measles

- Highly contagious paramyxovirus spread by coughing and nasal droplets
- Epidemiology:
 - Overall mortality 0.5%
 - Risk of infection 100% if not immunised
 - Epidemics occur every 7 years
 - Incidence up to 3000 notifications in epidemic years. Lab confirmations drop in epidemics as high incidence → high PPV of clinical diagnosis. Very few cases in non-epidemic years will actually be measles
- Presentation:
 - Incubation 10 – 14 days
 - Fever, ALWAYS a cough (“measles bronchiolitis), coryza, conjunctivitis for 2 – 3 days
 - Then red maculo-papular rash beginning on face and spreading to rest of body. White spots on cheery-red buccal mucosa for 24 hours before rash (Koplik’s Spots) – pathognomonic
- Treatment: Supportive, antibiotics for 2ndary infection
- Complications:
 - Otitis media (10%)
 - Pneumonia (1 – 5%)
 - Encephalitis (0.1%): 15% die and 25% left severely disabled. 1 in 100,000 develop the fatal grey matter degenerative disorder Subacute Sclerosing Panencephalitis (SSPE)
- Vaccine:
 - Live attenuated virus. Now MMR2 given at 4 years to ↑ time between epidemics and address 2 – 5% chance of primary vaccine failure in first dose
 - Mild fever, malaise or rash develops in about 1% 7 – 10 days after vaccination
 - 1 in 1 million develop encephalitis (1,000 fold less likely than if infected with wild virus)
 - Contraindicated during pregnancy and in immunocompromised hosts

Mumps

- Contagious paramyxovirus spread by saliva and droplets
- ~ 80 notified cases per annum. Used to be 3 – 4 year epidemics, now longer
- Presentation:
 - Incubation 2 – 3 weeks
 - 70% develop fever and swelling and tenderness of salivary glands
 - 15% have aseptic meningitis
 - 0.2% develop encephalitis
 - 20% of post-pubertal males have painful orchitis
 - Case fatality is 0.02% - usually from encephalitis
- Infective 1 week before and after parotid swelling starts
- Vaccine: Live attenuated virus (contraindicated during pregnancy and immunosuppression). Efficacy 95%. Only introduced because it can piggy back other vaccinations

Non-Polio Enteroviruses

- Include Coxsackie A and B, echoviruses and enteroviruses
- Cause: non-specific febrile illnesses, pharyngitis, gastroenteritis, viral meningitis, encephalitis, pericarditis, myocarditis, hepatitis, haemorrhagic conjunctivitis, etc
- Viral exanthem: macular rashes, maculo-papular, vesicular and petechial rashes
- *Hand, Foot and Mouth Disease:* Coxsackie A16. Mild illness, low-grade fever and sore throat. Scattered vesicular lesions in the mouth with similar lesions surrounded by erythematous areolae on the hands and feet.
- Incubation for 3 – 6 days, infectious for at least 1 week after onset of symptoms
- Diagnosis: culture (including from faeces – if isolates persist for several weeks may be unrelated to illness), possible PCR for blood and CSF. Serology difficult

Human Herpes 6 and 7 (Roseola Infantum)

- Acute febrile illness of young children for several days with occipital adenopathy, then reduced fever and appearance of a fine red maculo-papular rash over the trunk and arms for 1 – 2 days (confused with antibiotic rash)
- 70% of 2 year olds are sero-positive. Serology and PCR problematic due to latent infection
- Incubation 5 – 15 days
- Rare complications: encephalitis or benign intracranial hypertension

Erythrovirus (Parvovirus) B19

- = Erythema Infectiosum or Slapped Cheek Syndrome
- Mild illness, fever in 30%, bright red rash on cheeks for 2 – 3 days
- A few days later, a maculo-papular, then lace-like rash may appear on arms, then trunk, buttocks and thighs. May recur over following weeks after hot baths
- Incubation 4 – 14 days
- Infectious period is before the rash appears
- Complications: Adolescents and adults may also have polyarthralgia/arthritis, aplastic crisis if chronically anaemic (eg immunocompromised)

Orbital and Pre-Orbital Cellulitis

- Want to determine if its:
 - Orbital cellulitis:
 - Eg spread from anterior ethmoid sinus
 - Proptosis (eye pushed forward) and/or ophthalmoplegia (limitation of movement) and/or ↓ visual acuity
 - Surgical emergency: discuss with ENT, ophthalmologists, radiologist re imaging (CT not MRI)
 - Bugs: S Aureus, also S pneumoniae, S pyogenes, HIB
 - Cefotaxime and flucloxacillin
 - Complications: intracerebral extension (lumbar puncture contra-indicated until this is ruled out)
 - *Periorbital cellulitis*: in superficial fascia around the eye but not into the orbit. Fever and local tenderness
 - Investigations: FBC, blood cultures
 - S pyogenes and S aureus especially if contiguous skin lesion, S pneumonia, HIB if not fully immunised (can check urine for antigens). If HIB then ?HIB meningitis and Rifampicin prophylaxis for patient and family
 - Treatment:
 - If < 5 and not fully immunised: cefuroxime or Cefotaxime (50 mg/kg/6hr, max 2 g)
 - If > 5 or <5 and fully immunised: flucloxacillin (50 mg/kg/6 hr, max 2 g)
 - If no response after 24 – 48 hours, treat as for orbital cellulitis or underlying sinus disease
 - Local allergic reaction: eg just erythema without tenderness or temperature

Paediatric Orthopaedics

Congenital Abnormalities

Cleft Lip and Palate

- Failure of fusion of maxillary and premaxillary processes during week 5. With cleft lip, the lesion runs from the lip to the nostril, can be bilateral
- Incidence: 0.8 – 1.7 per 1000
- Cause: genes, drugs (benzodiazepine, antiepileptics), rubella
- Treatment:
 - Feeding with special teats
 - Surgery: repair lip at 3 months old, palate at 1 year old
- Prognosis: Unilateral or incomplete → good results. Bilateral lesions → some residual deformity
- Complications: otitis media, aspiration pneumonia, speech problems (refer to SLT)

Developmental Dysplasia of the Hip

- Encompasses Congenital Dislocation of the Hip

- Occurs after birth. Covers a spectrum from instability through subluxation to dislocation
- Commoner on the left. 25% bilateral
- Incidence: 1 in 1000
- Risk factors: extended breech, females, positive family history, first child, post-maturity, oligohydramnios
- Clinical: From 12 months shortening of the limb, external rotation and asymmetrical skin creases. Delayed walking, Trendelenburg gait and OA in early 30s
- Diagnosis:
 - Ortolani's Test: Flex hips to 90° then abduct them → click as femoral head slips back into the acetabulum
 - Barlow's test: Test for instability. Fix the pelvis with one hand and try and press the head and neck of the femur backwards out of the acetabulum
- Investigations. Neonatal ultrasound. > 4 months then xray
- Treatment: achieve and maintain a stable reduction. Neonate Pavlik harness. Later: open reduction
- Prognosis:
 - The earlier the treatment the better the outcome. Otherwise degenerative changes in the femoral head (eg anteversion), acetabulum, capsule, altered alignment
 - Poor prognosis: boy, late detection, Ortolani's negative (ie doesn't reduce easily)
- Clicking: a common finding and rarely associated with CCH

Club Foot

- Congenital Talipes Equinovarus
 - Small foot at birth, plantar flexed (equinus), heel in varus, forefoot displaced towards midline, fore foot inverted and lateral border convex, ankle is fixed, calf is wasted
 - Incidence: 1 in 1000. Twice as common in boys. 50% bilateral. Associated with other abnormalities (eg myelomeningocele)
 - Aetiology: multifactorial inheritance
 - Treatment: early diagnosis, stretching and strapping then serial casting from 10 days. Surgery at 12 weeks if not right yet to release tight tissues (eg tendons) on inner side of foot. Raised outside of shoe when walking. Follow-up: prone to relapse
- Calcaneo-Valgus Foot: Dorsiflexed and heel in valgus

Tarsal Conditions

- = Peroneal Spastic Flat Foot (old term)
- An abnormal union between one or other of the bones of the hind foot
- Autosomal dominant failure of segmentation or maturation of the mesenchyme
- Incidence 1%
- Diagnosis: flat foot as child with increasing stiffness of the hind foot. Progressive onset of pain in adolescence
- Diagnosis: lateral and oblique x-rays. MRI
- Treatment: 6 weeks casting, rigid orthosis, resection of the bar if found early, otherwise fusion

Internal Tibial Torsion

- Internal bowing of the tibia caused by intra-uterine positioning
- Exclude other problems of hip, knee and foot
- Usually self corrects by age 5

Femoral Anteversion

- ↑ Angle between femoral shaft and neck – normal is 15 degrees
- Exam: intoed gait and excess internal rotation of the hip. Egg-beater running style
- Treatment: Trend to correct up to 5 years of age. Avoid sitting with legs in internal rotation. Osteotomy if deformity is severe and does not correct

Scoliosis

- Lateral spine curvature
- Types:
 - Non-structural or postural curves, eg due to limb length inequality (curve disappears on bending forward)

- Structural curves: has lateral deviation *and* rotation of the vertebra. When child bends forward there is a hump to one side and curve is still present/exaggerated eg congenital, neuromuscular, miscellaneous
- Idiopathic types often present during adolescent growth phase
- Causes pain, deformity and impaired lung function
- Usually progressive. Follow carefully or active management (casts or surgery)

Other Congenital Skeletal abnormalities

- Neurofibromatosis:
 - Commonest single gene disorders – autosomal dominant
 - NF1, 1:3,500
 - NF2, 1:50,000
 - Neurofibromatoma, Café au lait, scoliosis, skeletal overgrowth, tibial bowing, thinning, fracture
 - See Neurofibromatosis, page 334
- Osteochondritis juvenilis (osteochondrosis): bony centres in children/adolescents become temporarily softened → deformity due to pressure → harden again in 2 – 3 years in deformed shape
- Skeletal dysplasia: achondroplasia, osteogenesis imperfecta, plus numerous others
- Soft tissue disorders: Marfan's, plus numerous others
- Chromosomal disorders: Trisomy 21, 13, 18
- Metabolic: Numerous, including Wilson's, haemophilia
- Neuromuscular: Charcot Mari Tooth, Duchenne, Cerebral palsy
- Spinal dysraphism

Bone and Joint Injury and Infection

- See Joint and Bone Infections, page 259, for Infection
- Differential of joint swelling:
 - Acute rheumatic fever
 - Septic arthritis
 - Reactive arthritis
 - Henoch-Schönlein Purpura
 - Juvenile chronic arthritis
 - Sero-negative arthritis
 - Rickets and vitamin deficiencies: A, folate, B12, C
 - Transient synovitis
 - Trauma
 - Haemophilia
 - Osteomyelitis

Supracondylar Humeral Fracture

- Most common fracture above the elbow, typically extension injury by fall on outstretched hand
- Type 1: undisplaced. Type 2: displaced but some cortical contact. Type 3: Completely displaced
- Complications: nerve palsy (usually resolves after 6 - 8 weeks), vascular injury (esp brachial artery), compartment syndrome
- Treatment: closed reduction and percutaneous pin fixation. Non-displaced fractures without collapse of the medial or lateral columns can be treated by immobilisation. Open reduction if unsatisfactory closed reduction, open fracture or if vascular compromise

Medial Epicondyle Fractures

- Often accompanied by dislocation. Bony fragment may be trapped in the joint preventing reduction
- Usually treated non-surgically

Fractures of the Forearm

- 75% are fractures of the distal radial metaphyses. Loss of reduction in 1/3 of cases

Wrist and Hand Fractures

- Radius and ulnar fractures account for 45% of childhood fractures
- Scaphoid fractures account for only 0.45% of paediatric upper extremity fractures
- 75% of finger injuries are stable and can be treated with simple immobilisation (often little finger)

- In toddlers and young children, most common pattern of injury is a crush injury of the finger, leading to distal phalangeal fracture, nail bed laceration and/or distal tip amputation
- In teenagers, diaphyseal level phalangeal fractures are common, with malrotation most apparent with digital flexion
- In teenagers, fractures of the metacarpal neck are common (“Boxer’s Fractures”)
- Fingertip trauma may lead to complete or incomplete amputation. Various treatment approaches. For more proximal amputations, replantation is now standard over 1 year. Best prognosis with sharp injuries (more common in adolescents, crush more common when younger)
- See also Forearm and Hand, page 247

Transient Synovitis of the Hip

- Transient synovitis is common and self-limiting, often following URTI.
- Hip or knee pain, limp, decreased motion but normal xray
- Main differential: septic joint. If in doubt, aspirate

Slipped Upper Femoral Epiphysis

- Most common disorder of the hip in early adolescence, especially overweight and boys
- 90% are chronic and stable (can bear weight) with limp for several months
- Pain on abduction, flexion, internal rotation
- Often pain refers to the knee
- Treatment: Percutaneous fixation

Femoral Shaft Fractures

- Common, generally solid healing
- Various treatment options including spica casting and traction
- Subsequent limb overgrowth is common but not predictable

Limb Length Inequality

- Various causes: check for soft-tissue hypertrophy, vascular anomalies, etc etc
- Often idiopathic. If mild (< 1.5 cm) then monitor with serial exam and x-rays
- Treatment depends on severity – involves surgical, gait, etc

Other

- Legg-Calve-Perthes Disease: Poorly understood. Typically affects *boys* 4 to 8 years. Osteochondritis and osteonecrosis of the femoral epiphysis. Softens bone then gradually reforms in a deformed shape. ?Due to interference with venous drainage of the femoral head. May present as an incidental finding. Treatment controversial. Younger the patient the better the prognosis. Usually benign. Maintain motion
- Knee injury:
 - Osteochondral fractures of the knee: associated with patellar dislocations
 - Osteochondritis Dissecans: Fragmentation or separation of a portion of the articular surface of the knee. Symptoms include vague pain, clicking, popping or effusion. Initial treatment is immobilisation
 - See also Knee Injury, page 255
- Physeal fractures of the distal tibia

Paediatric Neurology

Neurological Exam in Children

General (ALWAYS do these)

- Are they well or unwell (esp toxic)
- Growth:
 - Weight, height, and head circumference
 - Head exam:
 - Anterior and posterior fontanelles (while upright). Anterior closes ~ 18 months, posterior ~ 4 months
 - Sutures, shape of head,
 - Check for shunts (subcutaneous tubes behind the ears),

- Auscultation over closed eyes and temporal are for bruit
- Dysmorphic features
- Neurocutaneous stigmata: marks on skin, port-wine stains, Care-au-lait spots, use Woods lamp to look for depigmented lesions if fair skinned

Higher cortical function

- Ask questions appropriate to child's age
- State
- Attention: serial sevens, repeat numbers
- Memory:
 - Dependent on attention, processing and storing, ability to access and ability to communicate
 - Immediate (repeat numbers), recent (3 items at 5 minutes but not visual things), remote (old teachers name)
 - Object permanence
 - Visual: geometric reconstruction
- Reading and spelling
- Speech: dysphasia and dysarthria
- Draw a man
- Following instructions
- Behaviour
- Right left discrimination (crossed)
- Name objects – visual agnosia
- Construction of complex geometric figure
- Cortical sensation
- Abstract thought
- Looking for:
 - Frontal lobe disturbances: personality changes, irritability, lethargy, sphincter incontinence, primitive reflexes such as rooting, grasp re-emerge
 - Temporal lobe disturbances: altered ability to read, write and understand speech, memory dysfunction
 - Parietal lobe dysfunction: sensory perception abnormalities, 2 point discrimination, graphesthesia, stereognosis, apraxia

Cranial Nerves

- 1: Olfactory: don't often test unless abnormalities in the same area. Rarely impaired. Check each nostril separately. Use chocolate, mint or vanilla essence.
- 2: Optic
 - Visual Acuity:
 - Babies: fix and follow, optokinetic nystagmus, blink reflex (50% of 5 months, 100% by 1 year)
 - Toddlers: offer toys of different sizes. Look in books for smaller and smaller things
 - Visual Fields:
 - Screen first: objects in the periphery – make sure they can't follow your arm to your hand
 - If suspicious: test with wiggly finger ('look at my nose and grab the finger that wiggles')
 - Optic disc:
 - Very important
 - Use low light and small aperture
 - Get mum or dad to make funny faces behind you
 - Stay still and wait for optic disk to come into view
 - Look for venous pulsations – take pulse to get rhythm. If still can't see them, push lightly on orbit – if veins collapse then OK. If no pulsations then ?↑ICP.
 - Pupils
- III, IV and VI: Oculomotor, Trochlear and Abducens
 - Ptosis: nerve II and sympathetic. One eye doesn't open as much as the other
 - III: down and out
 - IV: Up and out
 - VI: in
 - Sun-setting: paralysis of upward gaze = pressure on quadrigeminal plate
 - Get them to follow an object past the limit of head turning – don't hold head

- Hold them to your stomach and spin around with their head out. Nystagmus is normal
- Dolls eye
- V: Trigeminal
 - Motor: temporalis – bulk, power, clenching, chewing. Get them to bite on a wooden spatula while you pull it away
 - Sensation: test from out of sight with feather
 - Reflexes: jaw and cornea (only if unconscious or other signs point to a problem)
- VII: Facial
 - Taste: anterior 2/3: very hard in children
 - Lacrimation and salivary glands
 - Motor:
 - Tickle nose with tissue (try and get them to wrinkle face up)
 - Close eyes/mouth open: look for asymmetry of facial creases
 - Watch when crying – emotional movements less affected than voluntary ones (helps localised to UMN/LMN)
- VIII: Vestibulochoclear
 - Ask parents
 - Testing: whisper words (ice-cream, Wiggles) – rub fingers next to other ear (\rightarrow white noise)
 - Spinning
- IX and X:
 - Symmetry of uvula and palate movement
 - Swallowing
 - Gag: only if really necessary
 - Taste on posterior tongue: too hard
 - Voice: nasal ‘b’, ‘d’ and ‘k’, hoarse
- XI: Accessory shrug shoulders, turn heads with resistance
- XII: Hypoglossus: stick out your tongue at me – bulk, fasciculation, power. Poke tongue through cheek and feel it

Motor

- Observe:
 - Abnormal movements: ticks, seizures, chorea, etc
 - Bulk
 - Scars
 - Contractures
 - Symmetry (eg small thumb nail on one side – contra-lateral parietal lesion)
 - Posture: eg frog leg posture in hypotonia, fisting
- Tone:
 - Must be relaxed. Lie on back and shake arms and legs to a song
 - Range of movements: passive and active
- Power:
 - Functional: Observe, including:
 - Gait: walking forward and backward, running, hopping, tandem gait (eg heel-to-toe), on tiptoes, on heals, on insides and outsides of feet (Fog test). Look for dystonic posturing of hands while they do this.
 - Proximal weakness: up steps, Gower’s sign, wheelbarrows, play ball, push-ups. Gower’s: lie on back – tell them to get up as quick as they can when you say ‘go’. Muscular dystrophy will roll onto front then climb up legs.
 - Handedness
 - Formal strength testing (grade 5 down to 0): Pull a toy, push me away, crazy glue (pretend to stick their finger to their nose and then try and pull it away), resistance, squeeze fingers
 - Pronator sign
 - Remember:
 - Proximal weakness: myopathy
 - Distal weakness: neuropathy (except myotonic dystrophy)

Reflexes

- Must be relaxed, be patient
- Hit your hand, not the child

- Test ankle jerk on the sole
- Swing with gravity, don't bash
- Use distraction (look over there...) and reinforcement: clenched teeth (chewing sticky lolly)
- Check for clonus
- Primitive reflexes (go at various ages): Moro, ATNR (atonic neck reflex) – turn head suddenly → extend arm on that side, Babinski

Sensation

- Difficult
- Test from out of range
- Test with a broken spatula: show them sharp and dull and then always use sharp
- Touch, pain, vibration, proprioception

Cerebellar

- Gait: Walk along a line on the floor – should be able to do it well by 6
- Rhomberg
- Finger nose: reach for toys (make sure they stretch)
- Foot tapping
- Rapid alternating movement
- Hands outstretched with eyes closed, look for drift

Head Size *

Microcephaly

- Head circumference below the 3rd centile with abnormally slow head growth
- Incidence: 1/1000, recurrence in siblings 1/50
- Causes:
 - Familiar: not associated with developmental delay
 - Autosomal recessive condition, associated with severe learning delay
 - Congenital infection: Rubella, CMV, Toxoplasmosis, Varicella Zoster, Listeria, Syphilis
 - Brain insult: eg perinatal hypoxia, neonatal meningitis. Likely to be accompanied by cerebral palsy, seizures, visual impairment, etc
 - Fetal Alcohol Syndrome

Large Head

- Megalencephaly = oversized brain
- Hydrocephalus: dilated cerebrum:
 - ↑CSF volume associated with ventricular dilatation and ↑intraventricular pressure
 - Due to:
 - Aqueduct obstruction: injury, infection or genes
 - Arnold Chiari Malformation (downward displacement and elongation of hind brain, with herniation into the cervical canal)
 - Acquired causes: meningeal adhesions, mass lesions, etc
- Chronic Subdural Haematomas
- Hydrencephaly: no cerebrum
- Benign familial anatomic megalencephaly or macrocephaly
- Metabolic Megalencephaly: late manifestation of many cerebral degenerative disorders (eg lysosomal storage diseases)
- Neurofibromatosis
- Cerebral Tumour

Headaches

- History:
 - Pain characteristics: how bad, do they vary from one to the next, throbbing (migraine)/tight (tension)
 - Auras: visual, unilateral slowly spreading tingling/numbness/weakness
 - Photo & phonophobic
 - Look pale/unwell →?migraine
 - Late afternoon →? hypoglycaemic

- Suspect ↑ICP if vomit in the morning (without much nausea), increasing severity, or wake in the morning or at night with a headache
- Stress: relationship to headaches to school and holidays
- Relieving factors: Sleep, medication
- Associated with migraines:
 - Motion sickness – patient and family
 - ‘Ice-cream’ headaches – like shooting pain into head when biting an ice-block
 - Benign Paroxysmal Vertigo of Infancy (not the same as adult BPPV): 2 – 3 minute episodes of unsteadiness, queasiness, nystagmus
 - Cyclical vomiting
 - Abdominal migraine
- Past Medical History: head injury. To assess severity ask: did he lose consciousness, did he go to hospital *and* stay overnight, have any stitches or need imagining
- Family history:
 - What kinds of headaches do the rest of the family get (don’t talk about migraine – different meanings to different people)? There is a family history in 80% of migraine sufferers
 - Serious neurological disorders, strokes
- Exam:
 - General: Well/unwell, growth (if big head then measure parents), dysmorphic features, skin (stigmata)
 - BLOOD PRESSURE
 - ↑ICP: ↓venous pulsations in retinal veins, papilloedema, ↓visual acuity, 3rd and 4th nerve palsy
 - Focal neurological signs: especially cerebellar (common site of lesion in kids 2 – 10)
 - Cranial bruit to check for AVM: common finding. Interested in asymmetry, or if it can be eliminated by compressing the ipsilateral carotid artery
 - Check sinuses, teeth, TMJ
- Differential:
 - Is it acute or chronic, recurrent or progressive, etc
 - Migraine: normally throbbing. ↑when stressed. Most common cause in children
 - Tension headache: Rare before adolescence. Presentation: constant daily bilateral headaches without well defined onset and ending, less impairment of function. Stress (ie doesn’t differentiate from migraine. But children usually somatise rather than tense up). More common in older girls
 - ↑ICP
 - Drugs: eg daily use of analgesics
- Management:
 - Reassure: most parents seek help to check its not serious
 - Education: Migraines are familial, due to ischaemia and vasodilation (which stretches pain fibres in blood vessels)
 - Symptom diary: check for food association (fairly rare)
 - Avoid triggers
 - ?Psychologist referral:
 - ↓Stress, get to the bottom of stress problems, relaxation, coping
 - It will be life long – learning skills to cope better than life long medication
 - Medication:
 - Paracetamol: need a big dose and right at the start to make a difference (otherwise ↓gastric motility and fail to stop spread)
 - Propranolol: tested in RCT, but not if asthmatic
 - Ergotamine: contraindicated if complex migraine (focal neurological signs)
- Migraine Definition:
 - Recurrent paroxysmal headaches with pain free intervals with normal health, plus two of:
 - Unilateral pain, nausea, visual or other aura, family history in parents or siblings

Seizures

- See also Epilepsy, page 133
- Classification:
 - Either partial or generalised
 - And one of:

- **Acute symptomatic:** any person in that situation would seize eg hypoglycaemia, heatstroke, meningitis, hyponatraemia. Seizure will stop when cause goes away (unless scarring – when it becomes a ‘remote symptomatic’ seizure)
- Single
- Benign Febrile Convulsion
- **Epilepsy:** Repeated unprovoked seizures
- If Epilepsy then:
 - Localised: Idiopathic, symptomatic or cryptogenic
 - Generalised: Idiopathic, symptomatic or cryptogenic
 - Unclassified
- Seizures:
 - A symptom – not a diagnosis or a disease
 - Hyper-synchronous excessive discharge of CNS neurons associated with a clinical sign
- Diagnostic process:
 - Is it a seizure or not
 - What type of seizures – is it generalised or localised, etc
 - Is it a single seizure, acute symptomatic, afebrile or epilepsy
 - If epilepsy, what syndrome is it (this step is critical to treatment and prognosis, but often ignored in practice)
 - Brain tumours cause 1 – 2 % of all seizures in children, and 4 – 6% of partial seizures
- Neuro-imaging:
 - Indicated for:
 - Neurological deficit/asymmetry
 - Neurocutaneous syndrome
 - Developmental regression
 - Partial seizures
 - Infantile spasms or myoclonic seizures in 1st year of life
 - Persisting unclassifiable seizures
 - Not indicated for:
 - Idiopathic generalised epilepsy
 - Benign childhood epilepsy with centrotemporal spikes (Rolandic)
 - Simple Febrile Seizures
 - CT:
 - Initial scanning technique for exclusion of tumour
 - Show calcification
 - Available and easier to perform
 - MRI:
 - Preferred imagining technique
 - Sensitive to migrational abnormalities or very small lesions
 - PET/SPECT scan: localise lesion on the basis of metabolism. Only if considering epilepsy surgery

Epilepsy in Childhood

- Incidence: 0.5 – 1 %
- Lifetime prevalence of a seizure is 5%
- Aetiology:
 - Idiopathic: normal kids, no structural abnormality, often family history, EEG normal, generally benign and good prognosis. Cause is assumed to be genetic – usually a channelopathy
 - Symptomatic: An underlying cause is known, and there are usually other signs of a problem
 - Cryptogenic: There are other problems besides seizures, eg retardation, focal signs, etc, but can't find a cause
 - Symptomatic and Cryptogenic: abnormal children, abnormal background on EEG, prognosis not so good and often seizures difficult to control
- Benign focal (Rolandic) Epilepsy of Childhood:
 - = Benign Childhood Epilepsy with Centrotemporal Spikes
 - Commonest focal seizures in children
 - Onset 3 – 10 years
 - 80% focal, especially mouth and face. 50% only have fits in sleep
 - EEG diagnostic. Prognosis excellent

- Childhood absence epilepsy:
 - Onset 4 – 10 years – often confused with daydreaming
 - Almost all outgrow the absence seizures, but 30% will have GTCS in adolescence
 - Usually easily treated
- EEG:
 - Need to do when sleep deprived and not on medication
 - 2 – 4 % of normal children have an abnormal EEG
 - 55% of epileptic children have an abnormal EEG
 - Looking at frequency, morphology, location, reactivity, symmetry, dysrhythmia, etc
 - Paroxysmal events:
 - Noises
 - Benign variants: associated with age and state
 - Epileptiform: inter-ictal and ictal
- Psychosocial aspects: More important than drugs. Peoples attitudes will do far more damage than a few seizures
 - Education
 - Counselling
 - Normalising
- Seizure precautions: when driving, swimming, bathing, scuba diving, etc
- Pharmacology:
 - Aim:
 - Seizure free with no side effects
 - Start low and go slow
 - Never stop abruptly
 - Start after 2 or more seizures
 - Stop after 2 years seizure free
 - Common drugs:
 - Carbamazepine
 - Valproic acid
 - Less common:
 - Clobazam
 - Ethosuximide
 - Phenytoin
 - Phenobarbitone
 - Rarer:
 - Vigabatrin
 - Lamotrigine
- Status Epilepticus:
 - Continuous or intermittent fitting > 30 mins
 - ABCDEFG – does airway need protecting
 - Give effective anticonvulsant – 2 doses of rectal diazepam, if it continues consider paraldehyde, phenytoin, general anaesthesia

Benign Febrile Convulsion

- Types of seizure occurring with fever:
 - Benign febrile convolution
 - Epilepsy: eg first epileptic seizure unmasked by fever
 - Acute symptomatic seizure: meningitis, etc
- Benign Febrile Convulsions:
 - Frequency: 2 – 5% of all children
 - Age: 6 months – 5 years
 - Temperature: usually > 38.5 C
 - Boys: Girls = 1.4:1
 - Family history common (polygenic inheritance)
 - Unrelated to prenatal and perinatal brain damage
 - Have seizures with fever *only*
 - Treatment:
 - Stop seizure: rectal diazepam (0.5 mg/kg) at home or in ambulance

- Find the cause of the fever: seizure won't hurt them but meningitis might!
- DON'T use anticonvulsants – decrease recurrences but potentially significant side effects to treat something that is benign
- Prevention: Avoid over heating. Paracetamol/ibuprofen or tepid sponging don't ↓risk of seizure
- Types:
 - Simple (75%): generalised, brief (< 15 minutes), does not recur in 24 hours
 - Complex (25%): Focal and/or prolonged and/or recurrence within 24 hours
- Recurrence: 30% will have a recurrence, 70% of these within the next year
- Risk of subsequent epilepsy:
 - Increased risk if neurologically abnormal prior, family history of epilepsy or first seizure is complex
 - Otherwise very slight increase in risk only
- Neurological sequelae:
 - No impact on behaviour, growth, IQ
 - Prolonged febrile seizures associated with hippocampal sclerosis (temporal lobe). Controversial. (eg which direction is causation)
- Parental education:
 - Seizure does not cause brain damage (if less than 30 – 45 minutes)
 - 30% chance of another seizure
 - Next time: stay calm, clear airway, recovery position when stopped (low tone), time the seizure
 - Call ambulance at 5 minutes:
 - Most seizures stop by 5 minutes – so those that haven't are more likely to go on for longer
 - Want to be at hospital and have it stopped by 45 minutes

Anoxic Seizures

- White breath-holding attacks:
 - Vaso-vagal events due to stimulus: eg anger, pain, vomiting, etc. [Big sympathetic drive → parasympathetic overcompensation????]
 - Occur in children from 2 – 10
 - Reflex *bradycardia* or brief asystole or peripheral vasodilation
 - Symptoms: pallor, ocular revulsion, don't breath, extensor posture, a few symmetrical clonic movements, spontaneous resolution and then fine
- Blue breath-holding attacks:
 - 1 – 5 years
 - Follow a stimulus, eg crying
 - Get worked up, don't breath in, run out of breath and don't breath in (actually stop breathing)
 - Cyanosis with retained heart rate
 - May lose consciousness and have some clonic movements
 - Blow on face to start breathing
- Both white and blue breath holders are often iron deficient → do dietary history and Hb test
- Don't treat them. Ensure parent isn't being manipulated by breath-holding by child

Tics

- Brief, sudden involuntary stereotyped purposeless movement involving the muscles of the face, extremities and trunk
- Worsens with anxiety
- May be able to be controlled for a short while
- Go away in sleep
- If florid, look like repeated myoclonic seizures
- Chronic Motor Tics:
 - Goes on for more than a year
 - Life long tendency
- Chronic Multiple Tics:
 - = Gilles de la Tourette Syndrome
 - Onset usually 2 – 15 years
 - Boys > girls
 - Tendency for life
 - Multiple motor and vocal tics which wax and wane

- Wide spectrum from minor → severe

Cerebral Palsy

- = A persistent disorder of posture or movement caused by a non-progressive, non-hereditary lesion of the immature brain, acquired either in utero or later at a time of rapid development of the CNS (up to several years after birth)
- May be accompanied by other impairments, eg retardation, vision defects or epilepsy
- Though lesion is static, the clinical features may develop for several years as brain function matures (may give appearance of being progressive – clinical signs have to wait until that part of the brain ‘kicks in’)
- Incidence:
 - Stable at about 2/1000.
 - 80/1000 for very preterm babies
- Stages of brain development:
 - Up to 20 weeks → major brain malformations:
 - Lissencephaly (brain without cortex)
 - Microgyria: lots of little indentations
 - Migration defects: islands of grey matter in the middle of white matter
 - 26 – 32 weeks: neurons climb glial fibrils: intense growth – prone to ischaemia. If born then, prone to germinal matrix bleeds. But ischaemia more important → Periventricular Leukomalacia (PVL)
 - Myelination starts at about 30 weeks, but most is after birth. Damage only becomes obvious as myelination complete (conscious control of arm at 4 – 5 months, leg at 9 months)
- Causes:
 - Anything that damages neurons: ischaemia, hypoglycaemia, infection, trauma, toxins
 - Only 10-30% attributed to “intrapartum asphyxia”. Normal PO₂ in utero is 15 – 25 mmHg ⇒ well adjusted to hypoxia
 - For many it’s due to an unknown earlier adverse event
 - Significant proportion preterm (43%)
 - Intrauterine Growth Retardation → ↑risk by 5 times
- Exam findings:
 - Hyperactive reflexes
 - Abnormal movements of chorea, athetosis, dystonia
 - Abnormal absence or persistence of infantile reflexes
- Differential:
 - Metabolic disorder
 - CNS degenerative diseases
 - Cerebellar dysgenesis or spinocerebellar degeneration

Classification

- **Hemiplegia:**
 - 0.79/1000
 - Congenital:
 - Spastic paralysis of arm and leg on same side. Arm usually weaker than the leg. Distal parts worse than proximal. Growth of affected parts reduced
 - Face not involved
 - Epilepsy common – correlates with degree of mental retardation (but IQ often normal)
 - Mechanism: vascular (ie stroke in utero). If preterm, usually periventricular rather than cortical and leg weaker than arm
 - Acquired:
 - Following infection, trauma, CVA, status epilepticus, etc
 - Most in first 3 years of life
 - Flaccid with facial involvement, spastic later
- **Diplegia:**
 - 0.9/1000
 - Spastic:
 - Problem in preterm 28 – 32 weeks
 - Follow bilateral periventricular injury, especially with hydrocephalus complicating, or injury to basal ganglia or parasagittal cortex

- Stiff lower limbs (may be floppy as neonates): flexion of hips and knees, scissoring (internal rotation and adduction), weak trunk and eventual contractures. May dislocate hips
- Upper limbs variably affected (if worse then more global)
- Hyperreflexia and spasticity with variable wasting
- Epilepsy uncommon, intellect may be retained (69%). Head growth mirrors intellect
- **Quadriplegia:**
 - Global cerebral insult: massive haemorrhage, shock, obstructed umbilical chord
 - Upper limbs often worse than lower, generalised spasticity and wasting.
 - Severe mental retardation, cranial nerve palsies, aspiration, etc
- **Athetoid:**
 - Extrapyramidal injury, especially perinatal insults (including kernicterus – unconjugated hyperbilirubinaemia)
 - Appears after 5 months: involuntary movements and posturing, poor trunk control, hypotonia or normal, normal reflexes
 - Impaired speech, drooling, facial grimacing, often deaf (especially high tone)
 - IQ often normal but difficulties communicating. Epilepsy in 25%
- **Ataxic:**
 - Cerebellar symptoms predominate
 - Cerebellum abnormal on imagining
 - Presents at 1 – 2 years, but floppy and docile from the start
 - Ataxia, intention tremor, late walking, high tone deafness, normal IQ in 50%
 - Can be familial disease
- Management:
 - Team approach: physio, OT, orthopaedic surgeon, etc
 - Prevent contractures and encourage normal developmental stages
 - Treat epilepsy
 - Rule out deafness, check special senses
 - Encourage communication
 - Prevent malnutrition
 - Encourage mobility and upright posture (frees up hands for ‘learning’ activities)
 - Support for child and family
 - Manage constipation, incontinence

Muscular Dystrophy

- Not common. Most common is Duchenne: 1 in 3,500
- X linked recessive, females usually asymptomatic. 1/3 new mutations
- Caused by failure to make dystrophin (in muscle cell membrane)
- Present with muscle weakness that is slowly progressive. Gower’s sign: proximal weakness → climb up their legs with hands to stand up
- Often mild intellectual handicap (IQ 85)
- Wheel chair bound by 12. ↓Respiratory function and ↑scoliosis → terminal bronchopneumonia
- Diagnosis: genetic tests, CK markedly elevated, myogenic pattern on EMG
- Treatment: supportive only

Acute Weakness in Childhood

- Consider:
 - Guillain Barre (LP shows elevated protein but normal cells), post-infectious (eg mycoplasma), often sensory involvement, treat with Ig
 - Transverse Myelitis: post-infectious, distinct spinal level, responds to steroids

Neural Tube Defects

- A neural tube defect – failure of closure of the neural tube (4 weeks gestation – often already happened by the time a woman knows she’s pregnant)
- At lower ends leads to spina bifida and at upper end anencephaly or encephalocele
- Rate varies on population. High in Irish, Welsh, Scottish (3%) and those from poor backgrounds (poor nutrition, ↓folate, etc)
- Multifactorial causes:
 - Genetic

- Environmental (eg diet)
- Drug associations (eg antiepileptics)
- Any midline lesion of the skin overlying the CNS from the nose to the sacrum may indicate a lesion below the skin (same embryological origin) – eg hair, pigmentation, etc

Types

- **Myelomeningocele:**
 - Most common: 90% of spina bifida, failure of caudal closure of neural tube → failure of closure of skin and absence/leaking of the dura/meninges.
 - Lumbar sacral (25%), lumbar or thoracolumbar (50%) or thoracic/cervical (11%).
 - Spinal cord opened out flat. Variable neuro deficit below lesion. Possible tethering
 - Leads to:
 - Paraplegia: paralysis of knee and hip extensors with retained flexion. Talipes (club foot) – equinovarus is commonest
 - Variable loss of sensation
 - Autonomic problems: faecal incontinence, dribbling urinary incontinence on lifting baby or spastic urethral sphincter (→ urinary retention), spastic bladder (→ reflux, hydronephrosis)
 - Open lesion → risk of ascending infection
 - Hydrocephalus: very common (Arnold-Chiari malformation). Dislocation of cerebellar tonsils and medulla into cervical canal, aqueduct stenosis (?primary lesion or tethering). Signs of hydrocephalus and ↑ICP: bulging fontanelles, rapid head growth, poor feeding, separation of sutures, ‘sun-setting eyes’ (looking down), drowsiness, venous congestion of skull. If acute: vomiting, bradycardia, hypertension
 - Management:
 - Interdisciplinary team
 - Close back to prevent infection
 - Drain hydrocephalus (ventriculoperitoneal shunt)
 - Bladder and bowel management
 - Review motor and sensory function, prevent contractures and aid mobility
 - Etc
- **Spina Bifida Occulta:** Range from failure of formation of dorsal spine (cord intact) to abnormal cord contents
- **Diastematomyelia:** bone or cartilage spur into the cord → progressive loss of spinothalamic function (pain and temperature) with growth (slices as spine elongates). Not common. Leads to regression of acquired skills.
- **Lipoma:** fatty mass → pressure effects
- **Tethered cord:** complication of many types. Cord fixed lower down and gets stretched as spinal column grows → loss of power, sensation and autonomic function (ie sphincter function, weakness in toes and forefoot, saddle anaesthesia)
- **Dorsal Dermal Sinus:** Epithelium lined tube from skin (lumbar/sacral) to dura or into spinal canal. Risk of meningitis (coliform) and tethered cord
- **Meningocele:**
 - Rarer. Swollen lesion on back, full of CSF, brilliant translumination. Little neurological deficit, risk of tethering
 - Cranial meningocele: occurs on skull and contains CSF
- **Encephalocele:** occurs on skull and contains brain. Prognosis more guarded
- **Anencephaly:** Failure of cephalic closure of neural tube → absence of cranium. Frequent polyhydramnios. Most live births die within 24 hours. Also occurs in other syndromes (⇒ always do karyotype)

Prevention

- Folic acid levels in pregnant women only half the recommended
- Recurrence after one affected child is 3 – 5% (?inborn error of folate metabolism)
- Low dose folate prophylaxis highly effective – but 50% pregnancies unplanned
- Adequate dietary intake hard (5 portions of broccoli a day!)
- Can detect with antenatal ultrasound or ↑maternal or amniotic fluid alpha-fetoprotein

Eye disorders in Children

- See also The Red Eye, page 142

- Routine eye checks for infants:
 - Fixing and following: ophthalmology referral if not doing this by 4 months
 - Pupillary red reflexes: view from about 50 cm. Leukocoria (white pupil) \Rightarrow ?retinoblastoma. Other irregularities \Rightarrow ?congenital cataract
 - Ocular alignment: symmetrical corneal light reflex (don't have to be exactly central). Strabismus (misalignment of visual axis) \rightarrow amblyopia. May be intermittent. Test with cover test. Accommodative Esotropia = convergent strabismus related to accommodation
 - Eye movements: if not following then test vestibulo-ocular reflexes using dolls eye
 - Adnexa Oculi: Eyelids. Check for Congenital Naso-Lacrimal Duct Obstruction (tears, puss or mucus discharged by pushing on lacrimal duct) due to incomplete canalisation. Most resolve by age 1 (\Rightarrow usually managed conservatively by twice daily lacrimal sac massage)
 - Globes and cornea: of equal size
- Serious disorders in the neonate (\rightarrow urgent referral):
 - Congenital Glaucoma: photophobia, corneal haze-opacity, corneal enlargement or asymmetry
 - Ophthalmia Neonatorum: conjunctivitis with infection and inflammation of the conjunctiva in first month of life. Urgent microbiology and iv antibiotics for chlamydia and/or N Gonorrhoeae
- Red Eye in Children
 - *Conjunctivitis*:
 - Common in newborns – may be serious
 - Bacterial: rapid onset, usually spills from one eye to the other. Puss.
 - Neonatal often Neisseria gonorrhoea (prevented with silver nitrate drops in new born if high risk). Can lead to perforation of orbit. If systemic spread then septic arthritis. Treatment: *B Penicillin 25 mg/kg/12hr iv + 3 hourly 0.5% chloramphenicol drops for 7 days*
 - 3 – 5 days post delivery: Chlamydia. Can progress to rhinitis and pneumonitis. Diagnosis requires special chlamydia swab. Treatment: *Erythromycin 10mg/kg/6hr po for 21 days* to eliminate lung organisms + *1% tetracycline drops*
 - Acute causes often Staph aureus, S pneumoniae, H influenzae or S pyogenes. Treatment: drops up to hourly (eg chloramphenicol)
 - Chronic: usually toxins or immune (eg Kawasaki, Erythema Multiforme, Reiter's Syndrome)
 - Viral: acute onset, often bilateral, minimal pain, thin watery discharge, photophobia. Adenovirus, Herpes Simplex, measles, etc. Generally clears spontaneously. If Herpes suspected (eg eyelid vesicles), start 4 hourly acyclovir and immediate referral
 - Allergic: history of atopy and itchy eyes. If mild then use astringent, topical anti-histamine or cromoglycate
 - *Subconjunctival haemorrhage*: common after blunt trauma (eg birth), coughing (eg whooping cough) and vomiting.
 - *Corneal abrasions*: trauma or infection (esp HSV)
 - Iritis/Uveitis: uncommon in children. May have no pain but strabismus or visual loss. Cornea red near iris (unlike conjunctivitis). Look for white cells in anterior chamber.

Renal Disease in Children

- See also Renal and Genitourinary, page 201

Proteinuria

- Definition: $> 150 \text{ mg protein/day}$ (same cut off as adults)
- Normally protein is lost from tubular cells. Pathological if:
 - Filtered protein from glomerulus
 - \uparrow Loss from tubular cells
- Categories:
 - Gross proteinuria: $> 1 \text{ gm/day}$ (\rightarrow nephrotic syndrome if severe)
 - Acute low grade
 - Chronic low grade
- Diagnosis:
 - Dipstick: measures concentration of protein, so if urine is concentrated $\rightarrow \uparrow$ protein concentration as well
 - 24 hour urine: problem if not continent

- Nephrotic syndrome:
 - = Proteinuria + oedema + ↓albumin in blood (hypoproteinaemia)
 - Oedema is due to ↓colloid osmotic pressure → ↑aldosterone → ↑Na → ↑H₂O retention → this leaks out as well
 - Caused by leaky glomeruli

Causes

- Minimal Change Disease:
 - See also Minimal Change Disease, page 213
 - = No change under light microscope
 - Passing up to 8 – 10 gm per day → gross oedema
 - 3 rare complications:
 - Hypoperfusion: classically the gut → abdominal pain
 - Loose Ig's as well → ↑risk of bacterial infection (eg pneumococcal)
 - Thrombosis (eg renal vein)
 - Usually grow out of it (eg over 6 months, although may persist until an adult). Unpleasant but not usually life-threatening
 - Treatment: steroids but side-effects
 - 10 – 20% have other causes which may → chronic renal failure
- Acute low-grade proteinuria:
 - No long term significance
 - Can be:
 - Exercise induced in some teenagers/adults
 - Urinary tract infection
 - Postural proteinuria (↑when standing up)
 - Have to demonstrate that it's gone (ie that it's not chronic)
- Persistent/chronic low grade proteinuria
 - Always have some. Exclude exercise and postural
 - Significant finding: ↑risk of renal disease, eg in adult

Haematuria

- Definition: > 5 RBC in high powered microscope field
- Categories:
 - Gross/Macroscopic:
 - UTI (most common cause by far)
 - Trauma: visceral damage easier in kids
 - Post-streptococcal glomerulonephritis
 - Stones
 - Wilm's tumour
 - Bleeding disorder (eg haemophilia)
 - Red food colourings (eg beetroot)
 - IgA nephropathy: IgA deposits on glomeruli
 - Acute microscopic:
 - Infection
 - Plus above list (which are more likely to be microscopic than macroscopic, and may be intermittent/chronic)

Acute Renal Failure

- = Acute renal 'success'. If kidney didn't shut down after ATN, would continue filtering at 1-2 l/hr with no reabsorption → very rapid dehydration
- Causes:
 - Ischaemia
 - Obstruction (eg congenital malformation)
 - Sepsis: toxins killing tubular cells + hypoperfusion
 - Drugs: at glomeruli or tubular cells
- Complications:
 - Fluid overload: fluid restrict to insensible losses (breath, stools, skin = 400 mls/m² of body surface) plus urine and vomit

- Hyperkalaemia:
 - No symptoms, so have to monitor
 - Treatment: salbutamol or insulin + glucose → shifts K into ICF
 - Calcium resonium: chelates K
 - Encourage anabolism with ↑ calories → ↑cell creation
 - Frusemide if any urine output
 - CaCl or Ca Gluconate: prevents arrhythmia
 - Dialysis
- Uraemia: vomiting, encephalopathy → dialysis
- Hypertension: due either to ↑aldosterone release or fluid overload

Chronic Renal Failure

- Incidence: 1 – 2 kids per million per year
- Disaster for families → very demanding treatment
- Causes:
 - Obstruction/congenital
 - Dysplasia (never developed normally)
 - Severe reflux
 - Glomerulonephritis
- Problems:
 - Nutrition (need ↑↑ calories → ?NG tube)
 - ↓Linear growth: due to ↓nutrition, ↑PO₄ → secondary hyperparathyroidism, ↓ vitamin D
 - Anaemia: due to ↓erythropoietin
 - Na/H₂O/K balance (may loose or retain too much)
 - Hypertension: angiotensin, overload, drugs
 - Ca balance
 - Development (always tired)
- Treatment: peritoneal dialysis

Genito-Urinary

Urinary Incontinence

- See UTIs in Children, page 221

Daytime incontinence

- History:
 - Previously continent?
 - Frequency, volume, urgency, pain, colour, continuous dribble (are nappies *never* dry - nearly always pathological)?
 - Infection history:
 - Associated symptoms
 - Past infections, kidney complications
 - Constipation (→ urinary retention due to pressure → infection). Need to fix bowels first
 - Family History
- Exam:
 - Palpable/distended bladder
 - Kidneys: palpable, tender?
 - Boy: examine penis carefully: balanitis (inflamed foreskin), constricted urethra
 - Girl: effusion of the perineum, can labia be parted
 - Signs of occult spina bifida (eg skin or vascular lesions over sacrum)
 - Are legs neurologically normal
 - **Blood pressure:** whenever risk of kidney disease
 - Screen for infection
 - Not PR
- Investigations:
 - Urine microscopy
 - Paediatric US referral
 - Further tests:

- Bladder volume scanning
- Paediatric MCU
- Cystoscopy
- Urodynamics
- If repeat infection:
 - ?Genitourinary malformation: do US or MCU to check for reflux
 - Infection leads to temporary scarring, which predisposes to infection. Break the cycle with prophylactic antibiotics

Bed Wetting/Enuresis

- Very common: 12% at age 6, 4% at age 14
- History:
 - Just at night time, or day as well (pathology more likely – must fix this first)
 - Is it primary or secondary:
 - Primary: have never been dry, most common, usually no associated pathology. No daytime problems. Pass large volume without waking. Ask about proportion of dry nights, getting worse or better?
 - Secondary: were dry, now wets (regression) → pathology common. Detailed history of when it began, pattern since then (\uparrow or \downarrow), symptoms of infection (dysuria, frequency), diabetes (weight loss, thirst), physical abuse. Can be induced by stress (eg starting boarding school, family disruption)
 - How much wetting: big patch, small patch. How often in the night (if several times then will take longer to come right)
 - Urinary symptoms: polyuria, dysuria, frequency
 - ?Constipation or soiling → need to fix this first
 - Family history (if one parent wet the bed, 40% of children will wet, if both parents then 80%). This is key information – normalises it for parents and child → \downarrow anxiety
 - Parents management style: punitive (unhelpful but common) or supportive (ignore wet pants, praise for waking to pass urine, not common but more helpful)
 - Previous treatment experiences
 - Expectations of parents and child
 - General developmental screen, including faecal continence, bladder training
 - Social history: how much extra support will the child or parent need to manage the treatment
- Exam:
 - End of bed: note weight loss, hydration
 - Growth
 - Lumbosacral area (midline defects → ?spina bifida), perianal sensation and neurological exam of legs
 - Abdominal palpation: kidneys, distended bladder, constipation
 - External genitalia
 - Blood pressure
- Investigations:
 - If primary then tests usually reveal nothing
 - MSU: blood, protein, glucose, casts, bacteria, urine analysis
 - May be: blood sugar (diabetes) and electrolytes (renal failure)
- Treatment:
 - **Reassurance:** a nuisance, but normal and curable. Not silly or on purpose. Primary enuresis is NOT a psychological problem, a personality disorder or ADD, but one of delayed maturation. However, stress will make a tendency to bedwetting worse
 - Parental intolerance will worsen it and \downarrow self-esteem
 - Avoid covert rewards (eg getting into parent's bed when their bed is wet)
 - No night nappy, leave lights on in toilet, normal fluids before bed
 - Convenient hygienic care of bed (eg waterproof under-blanket)
 - **Keep a diary** (good for any symptom):
 - Day, time of bed, hourly check till parents go to bed, size of wet patch
 - Helps keep accurate record and has therapeutic value (gives feedback, is something to do, etc)
 - Don't treat until age 6 or 7 – but do treat then otherwise psychological sequelae as they head into teens
 - Four options:

- Encouragement (rewards). See Behaviour Management, page 570
- Systematic Waking: wake half an hour before normal wetting time, and shift toileting time closer to bedtime/morning by half an hour a week
- **Pad Alarms:** Good ones best. Not funded. Parents need to be instructed on how to get maximum value from them. Explain and demonstrate to child. Hard work for parents as they must get up (take turns, may need extra support if solo parent). Must wake child properly (eg cold flannel on face). Relapse → immediate resumption of pad and alarm. Relapse reduced by over-training (once consistently dry, push fluids at bedtime, will recommence wetting but overcome it quickly)
- Bladder training exercises
- Which options:
 - Wets once or twice a week: Rewards for 4 weeks then pad and bell
 - Wets at the same time each night: systematic awakening
 - Wets many times through the night with small patches: bladder retraining and alarm
 - Wetting more than twice a week at unpredictable times: bell and pad
- If not improvement after two lots of 4 weeks then ?anatomical problem
- Not medication: Nasal ADH/vasopressin (specialist only) treats symptoms but doesn't change behaviour. Maybe useful for short term protection (eg school camps, etc)

Testes

Undescended testis

- = Cryptorchidism
- Descent complete in 96% at birth, in 99% at 3 months
- Premature will have ↑rate of undescended testis (5% at 1 year)
- Two types:
 - Arrest of descent: at internal or external ring, or at scrotal neck
 - Ectopic: outside of the line of descent
- May present with a hernia
- Surgical correction at about 12 months
- Sequelae of non-descent:
 - 20 times risk of malignancy
 - ?Impact on fertility (due to ?higher temperature impairs spermatogenesis)
 - If don't bring them down they may end up over the pubic ramus → very uncomfortable sex!

No testis

- If bilateral undescended testis and hypospadias → ambiguous genitalia → urgent referral
- Torsion in utero → no testis
- No testis = anorchia. Maybe no kidney on that side ⇒ check

Retractile Testis

- Normally in scrotum but retracts upwards during examination
- Testis normal size
- Follow-up 2 yearly
- Surgery unnecessary. Will drop into scrotum at puberty

Hydrocele

- Fluid collection between the layers of the tunica vaginalis secondary to trauma, infection or idiopathic. Implies a patent process vaginalis
- May be bigger in the evening than in the morning
- Transluminates well, is non-tender and non-reducible
- Herniotomy if not resolved by age 2. 50% disappear in first year. Remove tunica vaginalis → removes potential space
- Predisposes to hernia

Acute Scrotum

- Must examine the genitalia of every boy who presents with acute lower abdominal pain (may not localise to testis)
- In descending order of frequency, causes of an acute scrotum are:

- Torsion of the appendix testis
- Testicular torsion
- Idiopathic scrotal oedema. Symmetric swelling, no testicular tenderness. May include penis, inguinal and perineal regions. Exclude torsion
- Rarely, epididymo-orchitis
- Management of torsion:
 - High probability: short duration and negative urinalysis → surgery
 - Low probability: longer duration and positive urinalysis → ?Doppler US for ↓blood flow

Torsion of Appendix Testis

- Most commonly caused by Hydatid of Morgagni (Mullerian duct remnant) at top of testis
- Peak incidence at 10 – 12 years. Oestrogen stimulates enlargement of the remnants → predisposes to torsion
- Symptoms range from minimal inflammation to florid, swollen hemi-scrotum indistinguishable from testicular torsion
- Urgent surgical referral

Testicular Torsion

- Testes are covered by tunica vaginalis – has parietal and visceral surface (like lungs in pleura)
- Testis rotates on its chord within parietal tunica vaginalis
- Once torsion has occurred in one, more likely in another
- < 6 hours will probably not cause infarct
- Two peaks for incidence:
 - Neonatal: Testis usually dead by diagnosis. May not operate (will atrophy). May ‘pex’ contralateral side to prevent torsion
 - Age 13 – 15: History and presentation variable. Surgical emergency. If testis viable, untwist and fix. Fix contra-lateral side
- Need to remove a torqued testis, otherwise he will develop autoantibodies for spermatozoa → infertility of other testis

Epididymo-Orchitis

- Very rare in children. Two peaks
 - Newborn, with underlying urinary tract anomaly. Do US and MCU. MSU to rule out infection
 - In 13+ due to reflux up the vas → infection/inflammation
- Mumps orchitis does not occur in pre-pubertal boys

Penis

Smegma

- Yellowish coloured secretion-desquamation which occurs normally and keeps the foreskin separate from the glans
- May appear like a dermoid cyst underneath the skin
- Is normal, and will eventually extrude spontaneously

Retraction of the foreskin

- By age 4 most boys foreskins will be able to be retracted
- May have intermittent pain during separation of the adhesions and the foreskin may be red or swollen for a day or two

Phimosis

- Irretractable, scarred foreskin. May balloon on urination
- If mild, application of Betnovate ointment to the tight portion of the foreskin (retract loose bit to access it) is effective
- If ongoing problems → circumcision
- Paraphimosis: foreskin stuck behind glans → swollen. Always put foreskin back after catheterisation

Balanitis

- Infection of the foreskin, may remain distal or involve whole penile shaft
- Can be secondary to phimosis
- Treat with topical bactrim or oral antibiotics

Hypospadias

- Combination of dorsal hood, proximal urethral opening and chordee (central penile tilt)
- Presentation varies from mild to severe pено-scrotal type with ambiguous genitalia (check for testis)
- Correct at 9 – 12 months
- ↑UTIs
- ↑Infertility as the opening moves closer to the base of the penis

Ambiguous Genitalia *

- Relative complexity of male differentiation → vulnerable to wide variety of incomplete masculinisation
- History and exam:
 - Exposure to progesterone, testosterone, phenytoin, aminoglutethamide
 - Previous neonatal deaths
 - Phallic size, position of urethral orifice, fused labia, descended gonads
- Don't rely on appearances whenever babies have:
 - Bilateral cryptorchidism, even if there is a phallus
 - Unilateral cryptorchidism with hypospadias
 - Pено-scrotal or perineoscrotal hypospadius
- Causes:
 - Androgen resistance (extreme form: testicular feminisation)
 - Early in boys development, sertoli cells release anti-mullerian peptide → stops formation of the fallopian tubes, uterus and the upper 1/3 of the vagina
 - Testosterone and dihydrotestosterone from Leydig cells responsible for the rest of male genitalia. If a problem in this pathway → Girl with short vagina.
 - Present in puberty with primary amenorrhoea
 - Adrenogenital Syndrome:
 - Incidence: 1 in 14,000
 - Congenital adrenal hyperplasia: masculinised females
 - ↑Androgenic hormones because of ↓ 21-hydroxylase, 11-hydroxylase or 3-B-hydroxysteroid dehydrogenase
 - Can't produce cortisol → adrenal hyperplasia → overproduction of cortisol precursors → ↑androgens
 - Presentation: vomiting, dehydration and ambiguous genitalia. Hyponatraemia (with paradoxically high urine Na) and hyperkalaemia is common → may present with circulatory collapse in early life or hyponatraemic seizures (misdiagnosed as febrile convulsions)
 - Boys may present with precocious puberty or have ambiguous genitalia (reduced androgens in 17-hydroxylase deficiency)

Gastro-Intestinal

- See Appendicitis, page 167

Abdominal Radiology

- Should always be gas in the:
 - Stomach. If not, then ask why. ?Oesophageal atresia without fistula to the bronchus. ?To sick to swallow
 - Rectum
 - RLQ (Caecum)
- Gas bubbles. If only:
 - 1: pyloric stenosis. Do US to confirm (not barium meal)
 - 2: Duodenal atresia – “double bubble trouble”. Associated with Down's. Ante-natally: polyhydramnios (can't swallow)
 - 3: Jejunal atresia
 - Lots of bubbles but no normal caecal gas: Ileal atresia (Colonic atresia very rare)
- Other signs:
 - Gas on both sides of bowel wall → wall stands out as opaque line → Rigler's sign
 - Malrotation: wandering small bowel below duodenum with barium meal. If corkscrew then ?malrotation with volvulus

- Pneumatosis Intestinalis: gas bubbles in intestinal wall ('string of pearls'): if also in portal venous system (eg bubbles in liver) then necrotising enterocolitis

Congenital abnormalities

Tongue Tie

- Short lingual frenulum
- Rarely interferes with eating or speech
- Generally requires no treatment

Oesophageal Atresia

- Happens early in embryonic life:
 - Lots else happening then too – look for associations as well
 - Cardia, Renal, Anus, Vertebral, Oesophagus, Trachea: CRAVET
- Symptoms: dribbles all the time
- Usually distal oesophagus attached to trachea (fistula) → air in stomach
- Urgent neonatal repair

Pyloric Stenosis

- = Hypertrophic pyloric stenosis
- 4:1 boys to girls. Males 1/200 – 1/400
- Family history: in 15% of siblings or previous generation
- Pathophysiology: circular muscle hypertrophy → progressive narrowing of pyloric stenosis
- Presentation: 3 – 6 weeks, initial spilling → progressive dysfunction → several days of non-bilious high volume projectile vomiting with or between feeds. Dryish nappies (from dehydration)
- Exam: peristaltic waves of exaggerated gastric peristalsis + palpable lump in RUQ (= pyloric tumour) when hips flexed and relaxed (eg immediately after a feed)
- Differential:
 - Gastro-oesophageal reflux – but baby well and growing
 - Exclude infection: UTI, meningitis, gastroenteritis, chest infection
- Investigations: usually clinical diagnosis. Check electrolytes and blood gases for hypochloraemic hypokalaemic alkalosis
- Treatment:
 - Rehydration: IV saline + KCL + glucose
 - Surgery: pyloromyotomy

Duodenal Atresia

- Present in first 24 hours with green vomiting after feed
- Xray shows double-bubble sign: gas in stomach
- Associations: 1/3rd have Down syndrome, 10% of Downs have duodenal atresia

Small Bowel Atresia

- Due to loss of blood supply to that part of the gut in utero. Infarcts and heals (as opposed to after birth when bacteria → gangrene)
- Bowel distal to the obstruction may be malformed

Malrotation

- In 80% of cases, diagnosed in first month of life. Usually presents after 2 – 3 days with bilious vomiting
- Exclude: strangulated hernias, bowel obstruction secondary to adhesions, intussusception and sepsis
- Investigations: barium meal → duodenal jejunal junction hasn't ascended to level of pylorus and is not to the left of the midline
- Pathogenesis: Dates from time when the midgut is in the umbilical chord. Failure of fusion (sygiosis) of the small bowel mesentery to the posterior abdominal wall → narrow “universal mesentery” with the superior mesenteric artery supplying the whole mid-gut → torsion leads to mid-gut ischaemia
- Surgical emergency

Meckel's Diverticulum

- Most frequent congenital abnormality of the gut (2% of autopsied adults). Due to persistence of omphalomesenteric duct

- Illness of 2's: incidence 2%, 2 feet from ileocaecal valve, symptomatic from 2 years onwards
- Wide mouthed diverticulum (approx 5 cm), on antimesenteric border of the ileum, usually within 100 cm of ileocaecal valve. 30% of the time ectopic tissue is opposite the diverticular
- 50% have normal ileal mucosa, rest have duodenal, pancreatic, colonic or gastric (not subject to feedback → ulcers) mucosa
- Symptoms:
 - 40% of GI bleeds
 - Maroon not melaena
 - Intermittent
 - ↓HB but no shock
 - 30% present with intussusception or band, 20% with diverticulitis like appendicitis, 5% with umbilical mass
 - Meckel's diverticulitis: blocked, inflamed → enlarged → burst
- Rarely symptomatic after age 5, but may →
 - Haemorrhage, before age 10, due to peptic ulceration of surrounding ileal mucosa,
 - Inflammation, may mimic acute appendicitis
 - Obstruction in kids/teenagers: intussusception into lumen of bowel, or twist on fibrous remnant of the omphalomesenteric duct extending from bowel to abdominal wall (remnant of the yoke sac)
- Diagnosis and treatment:
 - Pertechnetate scan: looking for hot spot
 - Diagnostic Laparoscopy
 - Treatment with laparotomy and end to end anastomosis

Meconium Ileus

- Tenacious meconium won't shift, gets colonised and ↑gas
- ⇒ Cystic fibrosis. See page 615

Hirschsprung's Disease (Aganglionic Megacolon)

- = Aganglionic Megacolon
- 1st described by Hirshprung in 1886
- Incidence: 1 in 3 – 5,000 live births. Boys four times girls. Familial tendency
- Aetiology: ?arrest in migration of ganglion cells from neural crest down GI tract
- Pathology:
 - Absent GI ganglion cells (co-ordinate motility of bowel – Meissner's and Auerbach's plexuses). Always includes internal anal sphincter and spreads proximally a variable length:
 - 50% to recto-sigmoid junction, through to
 - 10% including total colon
 - Affected colon can't relax → greatly dilated proximal segment
 - Macroscopic: affected segment may look normal, proximal segment damaged mucosa, possible perforation, thickened wall
 - Microscopic: absence of normal ganglion cells (visible with acetyl cholinesterase stain) and hypertrophy of nerve fibres (non-specific – can occur with other conditions)
- Clinical presentation:
 - Age of presentation unrelated to length of affected segment. Eg someone with their total colon affected can present after years
 - 3 groups of kids:
 - Neonate: acute lower GI obstruction, abdominal distension, bilious vomiting, maybe fulminant diarrhoea, maybe perforation. Clue: no gas in rectum on x-ray
 - Infancy: constipation, abdominal distension, possibly precipitated by change in bacterial flora on introducing other foods after exclusive breast-feeding (may → massive diarrhoea)
 - Older: severe constipation, chronic abdominal distension, scybala (hard mass of faecal matter), failure to thrive, never soil pants
- Diagnosis:
 - Barium enema: narrow rectum, enlarged proximally. Usually rectum lumen twice the diameter of the colon. Don't do an enema if risk of perforation (barium in the peritoneum → serious peritonitis)
 - Rectal manometry: inflate balloon in rectum, distal rectum and internal anal sphincter should normally relax, this won't
 - Rectal biopsy: But finding ganglion cells is hard even in a normal specimen. Histochemistry – test for ↑Ach (preganglionic nerve cells looking for ganglion cells)

- Treatment: Two stage surgery:
 - Stage 1: Disobstruct: ostomy in lowest portion of bowel with ganglia
 - Stage 2: Later, bring ganglionated bowel to anus

Imperforate anus

- In girls, often attaches into the posterior wall of the vagina
- Adequacy of the levator sling depends on how high the lesion is. If low, only a superficial problem. If high (growth arrested above levator sling), then reconstruction is more difficult
- Look for other developmental abnormality: eg GU, vertebral, etc

Other

- Gastroschisis: paraumbilical defect with evisceration (extrusion of viscera) of abdominal contents. Incidence 1.6/10,000. No covering. Usually only bowel hanging out. Usually no other defect. Corrective surgery has good outcome. Delivery in tertiary centre
- Exomphalos: Herniation of abdominal contents (may include liver) into the base of the umbilical chord. Covered with peritoneum. Incidence 4.3/10,000. Other abnormalities often present

Acquired Causes of Obstruction

- In addition to congenital causes above (malrotation → volvulus, atresia, etc):
 - Hernias
 - Adhesions (always ask about previous surgery)
 - Intussusception
 - Volvulus

Intussusception

- Peak incidence 3 months – 2 years
- Usually ileocolic
- Causes:
 - 95% idiopathic
 - 5% mechanical: intestinal polyp, Meckel's diverticulum, lymphosarcoma (> 6 years old)
- Symptoms:
 - Often URTI 10 days before (→ adenovirus in Payer's patch)
 - Initial: severe abdominal colic every 15 – 30 minutes, very well in between
 - Later: red-current jelly stools, prostration, pallor (shock)
- Exam: sausage shaped mass → clinical diagnosis
- Treatment:
 - Hydrostatic reduction: blow air or barium up anus at 50% diastolic pressure. Not if small bowel obstruction or peritonitis (barium in peritoneum is nasty)
 - Surgery

GI Bleeding

- Causes:
 - Serious, life threatening bleeding rare: varices, stress ulcer, etc
 - Serious disease more common (the bleeding itself is not life-threatening):
 - Necrotising Enterocolitis (NEC)
 - Intussusception
 - Inflammatory bowel disease
 - Familial polyposis
 - Other differentials: Meckel's Diverticulum, A-V malformation, Anal fissure
- History:
 - Is it really blood? Is baby vomiting mum's blood (swallowed in delivery or cracked nipple), is it a UTI not rectal?
 - Do they have clotting problem? (Did they get vitamin K?)
 - How much, how fast

Hernias

Inguinal Hernia

- 4:1 male to female. 1% of boys

- Virtually all indirect. A widely patent proximal process vaginalis allows bowel (and ovary in girls) to enter the inguinal canal
- Presentation: intermittent swelling overlying the external inguinal ring that has been noticed by a parent
- 50% right, 25% left, 25% bilateral
- Do not resolve spontaneously
- If < 1 more likely to present with strangulation
- Incarcerated (bowel loop stuck through):
 - Peak incidence in first year – main cause of obstruction. High index of suspicion in any child with abdominal distress
 - If neglected will strangulate – testes will die first due to ↓venous return
- Management: Should be repaired ASAP.
 - 98% of acute or strangulated hernias can be reduced by taxis: manipulating it back in. Then fix electively (ie within a week)
 - If signs of ischaemic gut or peritonitis → surgery
- Complications:
 - Girls: fallopian tube and ovaries may be within the hernia. May tort. Care with surgery. Can completely close the internal ring.
 - Boys: damage to vas or testicular atrophy if surgery while acute

Umbilical hernia

- Rarely cause problems, even if large
- Repair at age 3 if haven't resolved by then

Congenital Diaphragmatic Hernia

- 1:5,000 live births. 1:2,000 total births (⇒ lots of still births)
- Diaphragm should close just before mid gut comes back from umbilicus. In this case, returning gut enters chest. Compromises ipsilateral lung development (more common on left) → mediastinal shift and lung hypoplasia
- Symptoms:
 - Early respiratory distress/cyanosis
 - Scaphoid abdomen
 - Bowel sounds in chest
 - Dextrocardia (diaphragmatic hernia most common cause)
- Treatment: don't bag the child → bagging also blows up stomach and guts → compromises lung expansion further. Ventilate. Surgery
- Complications: pulmonary hypertension in severe cases
- Overall survival of 40 – 60%

Common Childhood Presenting Chronic Symptoms

My Child Won't Eat

- Key issue: do they have normal growth:
 - Normal growth:
 - 1st year: go from 3.5 → 9 or 10 Kg
 - 2nd year: from 9 or 10 kg to 12.5 or 13 kg. Ie Growth slows markedly
 - Normal intake for first year:
 - 100 cal/kg/day
 - 150 mls fluid/kg/day
 - Breast milk has 67 cal/100 mls → 100 mls breast milk at 150 mls/kg gives 100 cal/kg
 - If normal growth – what are parent's perceptions of amount the child does and should eat. If perceptions not right then → stress, unhelpful dynamics around food (especially for strong willed child) → parents give them lots of milk so they at least get something → iron deficient
 - If not normal growth consider disease, congenital syndromes, are they being offered enough (eg maternal depression/anorexia). See Failure to Thrive (FTT), page 591

Reflux

- Symptoms: poor growth, vomiting, cry (especially after food), cough
- But:
 - All babies have some reflux

- All babies cry – parents may not realise how much is normal! Average baby peaks at 4 hours per day at 6 weeks, then declines. Is an association between crying and maternal depression
- Can measure pH via NG tube over 24 hours, or scope them (only in Auckland). But most babies with presentation of reflux don't have oesophagitis.
- If neuromuscular problems (eg Cerebral Palsy) then more likely to have problems with severe reflux oesophagitis
- Treatment:
 - Antacids, ranitidine, omeprazole
 - Crying decreases from 6 weeks – is this a treatment effect or normal development
 - Ensure good support: wider family, Plunket, etc
- See The Crying Baby, page 591 for Colic

Abdominal Pain

- ‘Functional’ pain (no organic cause) is ‘benign’:
 - Parents didn’t know until child said
 - Distractible from it
 - Central pain (point to umbilicus)
 - No sleep disturbance
 - No associated symptoms
 - Intermittent
- Organic causes mimicking functional pain:
 - Constipation (parents may not be aware that child has problem with constipation)
 - Abdominal migraine: migraine in 3 – 8 year old often presents as abdominal pain. Intermittent, goes pale, last an hour or two, not distractible. As they get older may develop into normal migraine. Check family history
 - Always examine genitalia in a boy with acute abdominal pain
- Other causes: appendicitis, intussusception, UTI, testicular torsion, volvulus secondary to malrotation, Meckel’s diverticulitis, renal colic, pyelonephritis, acute glomerulonephritis, drug ingestion, reflux oesophagitis
- Other causes are rare without associated symptoms (eg coeliac, Crohn’s)

Diarrhoea

- Is growth normal
 - Yes ⇒ no significant malabsorption:
 - Low grade infection, eg Giardia, Cryptosporidium
 - Diet, eg too much juice → overload sucrose absorption → osmotic diarrhoea
 - ‘Toddlers diarrhoea’: 18 – 24 months, sloppy poos 3 – 4 times a day. ?Variation of normal. Gets less messy/tiresome when toilet trained
- No:
 - Chronic infection: giardia, Cryptosporidium, parasites/worms
 - Immunosuppressed: any infection (eg Rotavirus, campylobacter etc) may become chronic
 - Coeliac: bloating, miserable, diarrhoea, signs of malabsorption
 - IBD: uncommon < 10 years. Abdominal pain, diarrhoea, blood in stool
 - Constipation → ?overflow diarrhoea

Encopresis/Constipation

- See also Constipation, page 177
- Definitions vary: mainly long term constipation/soiling pants, but may also include inappropriate toileting behaviour (eg going on the lounge floor!)
- Constipation is common
- The main issue is that hardness of the stool, not the frequency
- History:
 - Need information from both parent and child. Parent is unlikely to know about an older child’s toileting habits. Perhaps ask child while you’re doing the exam – that way parents are off to one side. “I’m going to ask you some really silly questions about your poos...”
 - Soiling (HPC): duration, frequency, severity, ever been continent
 - Associated constipation, withholding, absence of warning (likely), pain (eg fissure), associated wetting
 - Toileting behaviour: avoidance, motions in toilet rare

- Associated behaviours: hiding soiled underpants (common), scared of toilets at school, more serious conduct disorder (rare)
- Parent's management style: what's been tried, punitive (unhelpful but common), supportive (ignore soiled pants, praise for toileting, not common but more helpful)
- General developmental milestones
- Exam:
 - Inspection of perineum: situation of anus, dilated anus
 - Inspection of lumbo-sacral area
 - Neurological exam of the legs: (spina bifida), test ankle jerk (S1-2, anal reflex is S2-5)
 - Abdominal palpation: for palpable faeces
 - PR usually not necessary
- Differentials:
 - Fissure: usually secondary to constipation → vicious cycle
 - Drugs: morphine, codeine, leukaemia drugs
 - Hypothyroidism (NB: associated with Downs)
 - Rare causes: Spina bifida occulta, Hirschsprung's (ask about delayed passage of meconium), anal stenosis (often anal opening is more anterior)
- Pathogenesis:
 - Vicious cycle: chronic dilation of rectum, sigmoid and descending colon → ↓sensation of fullness → go less often → faeces dry out more → hard → don't completely evacuate → ↑distension → ↓strength → overflow diarrhoea (with no awareness)
 - Constipation is common post-gastroenteritis or after surgery
 - Can more rarely be due to food allergy
- Management:
 - Explain normal anatomy and function of the rectum. Use a diaphragm.
 - Explain process: withholding stool → dilated rectum → loss of normal sensation → no warning its coming → he's not being naughty and will take a while to come right (ie stick with treatment)
 - Test transit time by eating a pile of whole kernel corn and seeing how long it takes to come out the other end. The ideal is < 24 hours
 - Structured toileting programme: diary and reward system for sitting (take a book if they're bored) not for clean pants. Toilet for 10 minutes after each meal. Use timer
 - Fibre and adequate fluids to keep stools soft
 - Treatment of severe constipation:
 - Use enemas to completely empty bowel – get visiting paediatric nurse to do it – easier on Mum and Dad
 - Laxatives every day to empty bowel (eg lactulose, magnesium sulphate) + regular toileting. Coloxyl drops (a stimulant) may → colic in kids. Lubricants (eg paraffin oil) are good but not very palatable
 - Continue for weeks/months until rectum normal size again
 - Frequent visits for support of parents and encouragement of child

Gastroenteritis

Differential of acute vomiting/diarrhoea

- Enteric infection:
 - Virus: rotavirus (45% of acute gastro), also enteric adenovirus, caliciviruses, astroviruses
 - Bacteria: Campylobacter, Salmonella (more common spring/summer), also Yersinia, enterohaemorrhagic E coli, shigella
 - Protozoa: giardia, cryptosporidium, also microsporidia, amoeba
 - Food poisoning: (had anything different to eat from the rest of the family?) Staphylococcus enterotoxin, bacillus cereus, Campylobacter, salmonella, E coli, Norwalk virus
- Systemic infection: if sicker than history suggests then UTI, Pneumonia, otitis media, meningitis, sepsis (including meningococcaemia)
- Surgical conditions: Appendicitis, intussusception, bowel obstruction, Hirschsprung's enterocolitis, pyloric stenosis, incarcerated inguinal hernia, testicular torsion
- Other disorders:
 - Diabetic ketoacidosis
 - Antibiotic associated diarrhoea

- Haemolytic uraemic syndrome (renal failure, haemolytic anaemia and thrombocytopenia, eg due to E Coli verocytotoxin, also drugs, SLE, etc)
- Poisoning

Warning Signs

- Seek urgent advice if any of:
 - Vomiting bile or blood
 - Severe abdominal pain
 - Toxic appearance (ie more than just gastro): lethargy, poor perfusion, hypo/hyper ventilation, cyanosis
 - Abdominal signs: distension, tenderness, guarding, mass, hepatomegaly
 - Failure to thrive
 - Neonate

Diagnostic Clues

- Sudden onset of fever, vomiting and watery diarrhoea: viral gastroenteritis
- Cramping abdominal pain and frequent bloody, mucousy stools: bacterial gastroenteritis. If an infant and severe pain or pallor, consider intussusception
- Colicky pain, RIF pain, bile stained vomiting and distension → surgical case
- Season: Rotavirus during winter epidemics, giardia and cryptosporidium during the spring and campylobacter in the summer

History

- Vomiting: bile, blood, coffee grounds, volume, frequency, total duration
- Diarrhoea: nature, colour, consistency, blood, mucus, frequency, volume, total duration
- Amount and type of recent food and fluid intake
- Urinary output
- Other symptoms:
 - Fever
 - Abdominal, groin or scrotal pain
 - Urinary symptoms
 - Respiratory symptoms
 - Recent illness
- Other:
 - Antibiotics and other drugs
 - Infectious contacts
 - Possible contaminated food ingestion, including shellfish
 - Overseas travel in the last 2 months
 - Immunisation
 - Other medical conditions, GI, diabetes, heart or renal

Management

- Principles:
 - Dehydration is the most important complication. In infants it can appear in several hours
 - See Assessing fluid loss, page 650 for assessment of dehydration and rehydration
- Investigations:
 - Stool microbiology: Only if:
 - Blood in the stool
 - Recent overseas travel
 - Suspected epidemic or food poisoning
 - Child in an institution
 - Chronic diarrhoea (> 3 weeks)
 - Biochemistry: Na, K, Cr +/- glucose +/- ABG if severe, < 3 months, or on IV therapy
 - Other: urines, blood, and CSF culture, CXR, AXR, LFT etc if indicated
- Management:
 - Ambulatory if diagnosis not in doubt, family able to cope, have transport, no dehydration and good fluid intake

- Admission if: diagnosis in doubt, < 3 months, high risk, dehydration, failure to improve, pre-existing condition (get sicker quicker: eg Ileostomy, short gut, cyanotic heart disease, renal failure, diabetes, etc)
- IV Rehydration if: shocked, severely dehydrated, failed trial of oral therapy
- Treatment principles:
 - For a non-dehydrated child:
 - Small, frequent sips of Gastrolyte (doesn't fix diarrhoea) – not for bloody dysentery (dehydration not the biggest concern). 5 – 7 ml/kg/hr
 - $\frac{1}{2}$ strength formula feeds
 - Fruit juice diluted 1:4
 - Maintain nutrition: Get back to solids within 6 – 12 hours if possible: banana, apple, rice, potato, noodles, toast and vegemite
 - Breast-feeding is continued
 - **Do not** use anti-emetics nor anti-diarrhoeal agents
 - For a dehydrated child, see page 650

Lactose Intolerance

- Small bowel injury → temporary lactose intolerance
- Most common in bottle feed babies < 6 months. Uncommon in breast-feed babies.
- Clues are consistent fluid stools, or their restarting with reintroduction of milk feeds, excess flatus, perianal excoriation
- Testing: Collect 5 drops of stool from a plastic lined nappy, mix with 10 drops of water and add a Clinitest tablet. Colour reaction of > $\frac{3}{4}$ % indicates sugar is present
- Change to a lactose free formula for 3 – 4 weeks, then introduce the old feed over 2 – 3 days

Nutritional Deficiencies in Childhood

Iron Deficiency

- See Iron Deficiency Anaemia, page 288
- Commonest deficiency in NZ and worldwide
- Marker of poor diet generally
- Associated with:
 - Inadequate iron intake:
 - Homogenised cows milk
 - Late introduction of iron-rich foods
 - Prolonged sole breast feeding (> 6 months)
 - Intrauterine growth retardation and placental insufficiency (especially rapid catch up growth)
 - Excess losses: chronic gut losses (eg infestation, food intolerance) and skin loss in severe ectopic eczema
- Sources of iron:
 - Poor sources:
 - Spinach: poorly absorbed
 - Cows milk: poor source and may lead to gut bleeding
 - Breast milk: only sufficient to 4 – 6 months, but ↑ absorption once food is introduced
 - Good sources:
 - Meat: haem iron well absorbed. Especially dark red meat (eg liver)
 - Pulses: lentils, peas, baked beans and soya beans (not green beans), but ↑ gas
 - Dark fish, shell fish and spices
 - Breast milk and vitamin C ↑ absorption, Cows milk and tea ↓ absorption (NB some Polynesians call tea milo – so ask what sort of tea)
- Anaemia:
 - At birth, Hb = 170, several weeks later = 105
 - Clinical effects: tired, lethargic, irritability, slow cell mediated immunity, pica (eat anything) which may → lead poisoning (small RBCs and anaemia)
 - Diagnosis:
 - Look for pale **earlobes**
 - Blood tests, iron studies etc. MCV < 71 in child over 3 months
 - Ferritin low (but high if infection – test CRP as well and ignore ferritin if raised)

- Serum iron – altered in presence of infection. Zinc Protoporphyrin is a new, sensitive test (Zn substituted for Fe in haem).
- Reticulocyte count useful test of response to treatment. Should respond within a week
- Treatment:
 - Find and fix cause: if diet then → dietician.
 - Ferrous gluconate elixir: 50 mg/kg/day (= 6mg/kg/day elemental iron) in 2 – 3 doses with fruit juice until MCV normal

Rickets

- See Parathyroid, page 101
- Usually a lack of Vitamin D. With fear of sunburn, it is likely to increase
- At risk:
 - Pigmented people with low dietary vitamin D intake and low sunlight exposure. Breast milk is not a very rich source of vitamin D
 - Preterm infants with low Vitamin D intake
 - Fat malabsorption
 - Other rarer causes: anticonvulsant therapy, chronic renal disease, Ca or phosphate deficiency
- Diagnosis:
 - Clinical: broad wrists, tender joints, avoidance of weight bearing, bowed legs if weight bearing, bent pelvis (→ obstructed labour later in life), Ricket Rosary (swelling of costochondral junctions)
 - Lab: ↑ALP, ↓PO₄, Ca usually normal
 - Xray: Widened metaphysis and splaying of softened bones, generalised osteopenia
- Treatment:
 - 1-α cholecalciferol: 0.05 – 0.1 mcg/kg/day until ALP normal
 - Surgery to bones not usually necessary, even when very bent

Other deficiencies

- Breast Milk is short of:
 - Vitamin K (fat soluble). Deficiency → haemorrhagic disease of the new born in first few weeks/months
 - Vitamin B12: if mother is vegan → CNS symptoms (fits, abnormal movements, mental retardation) + macrocytic anaemia
- Chronic malabsorption or prolonged TPN → Zn deficiency → Acrodermatitis Enteropathica (rash, especially around buttocks) and immunodeficiency
- Vitamin A deficiency: from fat malabsorption or ↓ intake → night blindness and ↑risk of complications from eg measles
- Folic Acid: Deficiency during pregnancy → ↑ risk of neural tube defects

Food Allergy

- See also Allergy and Hypersensitivity Disorders, page 309
- Commonest in first years of life (gut less good at keeping allergens out)
- 5 – 6% of children cf 1 – 2 % of adults
- Commonest allergens: milk, eggs, peanuts, soy, wheat
- Mechanisms include:
 - IgE mediated – rapid onset, due to mast cell activation and histamine release
 - Delayed hyper-sensitivity
- Scenarios:
 - Urticaria/angio-oedema:
 - Rapid onset after contact with oral mucosa
 - Chronic urticaria rarely due to foods (except ?food colourings)
 - Confirmed by skin testing
 - IgE mediated
 - Risk of future anaphylaxis (systemic reaction distant from contact point).
 - Risk factors for fatal outcome: Asthma, peanut/nut allergy
 - Treatment: Adrenaline 0.01 ml/kg of 1:1000 im (10 mcg/kg) [relatively safe im, compared with iv, which risks tachycardia and arrhythmia so would only want to do it in cardiogenic shock]

- Atopic dermatitis: takes days to weeks following food exposure. Strong association between severe asthma and food allergy (60%)
- GI symptoms may be at any point in the gut: oesophagus (reflux), stomach (vomiting), small bowel (colic, diarrhoea, malabsorption) to large bowel (diarrhoea, gas, bloody stools, mucus, constipation)
- Respiratory symptoms: much less common with foods. Oral allergy syndrome: pollen allergic individuals may get oral tingling/swelling after eating some fruits/vegetables

Cervical Lumps

- 99% of general neck lumps are lymph nodes:
 - Large nodes can take up to 6 – 8 weeks to go down
 - Three types:
 - Reactive hyperplasia: due to infection, not painful
 - Acute lymphadenitis:
 - Acutely tender, erythematous mass with accompanying fever, usually settle with rest/analgesia
 - Results from URTI, cellulitis or other skin infections
 - Cervical lymphadenitis: S aureus or S pyogenes
 - Management: antibiotics and/or drainage
 - Lymph node abscess: lymphadenitis may progress to abscess. Doughy feeling. Overlying skin erythematous. If raised, red and soft →? Staph abscess → flucloxacillin (always on an empty stomach). Augmentin for Strep abscess. Otherwise excise and drain under GA
 - Rare causes of lymph node enlargement: Consider if subacute, minimal tenderness, fixed or overlying skin changes consider:
 - Cat-scratch disease
 - Toxoplasmosis
 - Cutaneous Tb (collar stud abscess, bruised looking, no systemic symptoms, non-tender, tethered to skin, 6 mths to 5 years): excision, Mantoux and chest x-ray
 - Hodgkin's Lymphoma: Child > 5, rapid enlargement, rubbery spherical lymph non-tender nodes, night sweats, fever, weight loss, lymphadenopathy elsewhere, splenomegaly
 - Lateral Neck Lumps: branchial cysts and branchial sinuses
 - Midline Neck Swellings:
 - Thyroglossal Cysts:
 - 80% of midline cervical lumps
 - Peaks in pre-school child and young adulthood
 - Swelling near the hyoid that moves with swallowing or when pokes tongue out
 - May trans-illuminate
 - Early referral: get it out before it becomes infected
 - Treatment: surgery (Sistrunk procedure) and excision of the tract
 - Submental nodes: Usually superficial and anterior. Check mouth for primary infection (eg ulcer)
 - Dermoid Cysts: Common at the corner of the eyebrow (external angular dermoid). In the cervical region they are subcutaneous and mobile, and appear yellowish. Require excision
 - Ectopic Thyroid: Rare. May be only thyroid tissue. Tend to become hypothyroid

Childhood Cancer

- Cancer: 10% of childhood deaths, most common cause of death after accidents ⇒ have high index of suspicion
- Distribution:

	% of cancers
ALL	23
CNS	21
Neuroblastoma (→ chemo)	7
Non-Hodgkin's Lymphoma	6
Wilm's (Kidney)	6
Hodgkin's Lymphoma	5
AML	4
Melanoma	2

- Signs and Symptoms:

- Often non specific
- Adult symptoms rare, eg epistaxis, dysphagia, non healing lesion, rectal bleeding, change in bowel habit
- Para-neoplastic syndromes are rare
- Headaches warranting investigation. Headaches are common, but watch out for:
 - Recurrent morning headaches
 - One that awakens the child
 - Intense and incapacitating
 - Headaches that change in quality, frequency and pattern (eg getting more frequent)
 - Focal signs or ataxia
 - MRI more sensitive than CT
- Lymphadenopathy:
 - Common finding in cervical, axillary and inguinal chains. Usually < 1 cm
 - Most enlarged nodes are due to infection
 - Suspicious if found in mediastinum, posterior auricular, epitrochlear and supraclavicular
- Bone and Joint Pain:
 - Early symptoms rarely include pain – except in bone (bone cancer and malignancy)
 - Usually no pathognomonic signs on Xray → need biopsy
- Pancytopenia:
 - Common finding in ALL and AML
 - Need neutrophil count specifically. ↑Lymphocytes may mask ↓neutrophils.
 - From 6 months to puberty, anaemia is 110 g/L. 50% of leukaemia presents with Hb < 75 g/L
 - Involvement of two or more lines → bone marrow evaluation
- Leukocytosis: Common in AML and ALL. But count may get up to 50,000 with septicaemia and some viruses, also in Down syndrome and post-natal
- Presenting signs of cancer:
 - Recurrent bone pain, paleness, weight loss: leukaemia
 - Morning headache with vomiting: brain tumour (usually a migraine)
 - Lump in neck not responsive to antibiotics: Lymphoma
 - White dot in new born eye: Retinoblastoma
 - Proptosis (bulging eye): Leukaemia, neuroblastoma
 - Swollen face and neck: lymphoma, leukaemia (compression of veins)
 - Abdominal mass: Wilm's, neuroblastoma, liver & spleen enlargement in leukaemia
 - Cough, stridor, haemoptysis, Horner's: Mediastinal tumour
- Diagnosis: tumour markers (only in neuroblastoma: catecholamine), imaging, bone scan, biopsy

Emergency Management

Assessing Fluid State

Assessing Vital Signs

- Rate is always subservient to quality:
 - Thready pulse: eg palpable at neck and groin only
 - Respiration: more important than rate are grunting, flaring, subcostal retraction, use of accessory muscles (in neonate → bobbing of head)
- Blood volume:

Neonate	90 ml/kg
Child	80 ml/kg
Adult	70 ml/kg

 - In a trauma situation, guess the weight: (age + 4) * 2
- Urine output:
 - In nappies: 2 ml/kg/hr
 - Toilet trained: 1 ml/kg/hr
- Normal fluid requirements in absence of sweating:

	Per hour	Per Day
First 10 kg	4 ml/kg	100 ml/kg
2 nd 10 kg	2 ml/kg	50 ml/kg
Each 10kg thereafter	1 ml/kg	25 ml/kg

- Nutrition: to maintain weight need 75 calories/kg/day
- Heat loss:
 - 70 kg person: surface to mass ratio is 0.02
 - 2 kg person: surface to mass ratio is 0.08
 - Rate of heat loss is proportional to (body temp – room temp) to the power of 4. Best way to maintain body heat is therefore to heat the room.

Assessing fluid loss

- Only reliable indicator is pulse. BP doesn't drop till severe dehydration (compared with adult where BP declines proportionately with losses)
- No physical signs until > 3% loss
- Most signs of dehydration are those of shock
- Change in body weight is the most accurate estimate of fluid loss – but is rarely available
- Dehydration in obese children is often under-estimated

	Mild	Moderate	Severe
Loss: total body weight	3 – 5%	6 – 9%	> 10%
Mental state	Thirsty, alert	Thirsty, lethargic	Drowsy, hypotonic
Skin turgor	↓	↓↓	↓↓
Mucus membranes	Dry	Very dry	Parched
Skin colour	Pale	Grey	Mottled
Urine	Oliguria	Oliguria	Marked oliguria
Blood pressure	Normal	+/- Normal	< 70 systolic
Peripheral temperature	Cool	Cool	Cold & clammy
Pulse	+/- ↑	↑	↑↑ & thready

- Assessing turgor: pinched edge of skin goes down slowly. Do centrally on abdomen, chest, thighs
- Also when severe: rapid, sighing respirations (Kussmaul breathing)
- Poor predictors of dehydration: Sunken eyes or anterior fontanelle, dry mucous membranes, absence of sweat or tears

Management of Non-Dehydrated Child

- If no or infrequent vomiting that is not interfering with fluid intake then 5 – 7 ml/kg/hour of:
 - Breast milk
 - ½ strength formula
 - Fruit juice 1 part in 4 with water
- After 6 – 12 hours introduce: bananas, rice, potato, parsnips, pumpkin, dry biscuits/toast with vegemite

Management of Mild-Moderate Dehydration

- Admit or observe in a short stay facility for several hours
- Don't use homemade solutions – use Gastrolyte
- Orally, or by NG tube if necessary:
 - Replace calculated losses over 6 hours (don't worry about maintenance requirements). Hourly observations and reassess and reweigh after 6 hours
 - Give the remainder of the daily fluid maintenance over the next 18 hours
- Resume breast feeding as soon as rehydration is complete or sooner if this takes longer than 6-hours
- If after 4 – 6 hours the child remains dehydrated, then IV

Management of Severe Rehydration

- **WEIGH THE CHILD** to assess progress
- 3 stages:
 - Initial bolus if necessary. 10 - 20 ml/kg of Ringers Lactate or normal saline over 10 – 15 minutes, reassess and repeat if necessary
 - Replacement + maintenance
 - Maintenance only
- Rehydration of isotonic dehydration:
 - *Replacement:* Normal saline (or Ringer's Lactate or Hartmanns – more physiological)
 - *Maintenance:* 1/5th normal saline + 5% Dextrose + 20 mmol/l KCl [Barts] (gives a bit much Cl but the kidneys can sort that)

- If initially shocked, do not add KCl until urine is passed. If they have ATN following shock (\rightarrow renal failure) don't want to overload K
- Timing:
 - Infuse replacement fluid over 24 hours with the first 24 hours of maintenance using *ongoing replacement*: $\frac{1}{2}$ normal saline + 2.5% dextrose + 10 mmol KCl (in 500 ml)
 - Monitor electrolytes before, and during, up to 6 hourly
 - Once they are able to tolerate oral fluids, treat as for mild/moderate dehydration
- Theme and variations:
 - Diarrhoea:
 - Lost Na, HCO₃, Cl and K from GI mucosal cells – replace slowly
 - Resuscitation with bolus of crystalloids, eg Ringer's lactate, normal saline
 - Maintenance with: $\frac{1}{2}$ normal saline + 2.5% dextrose + 20 mmol/L KCl
 - If persistent acidosis due to HCO₃ loss or lactic acidosis then add in HCO₃
 - Rehydration of **hypernatraemic** dehydration (eg serum Na > 150):
 - Often the result of administering hyper-osmolar fluids (eg sports drinks) with vomiting and diarrhoea \rightarrow greater water loss due to water sucked into GI from circulation then vomited/passed
 - Will be more dehydrated than they appear due to fluid shifts from ICF \rightarrow ECF
 - If shocked give 10 ml/kg boluses of normal saline until circulation restored
 - Calculate deficit
 - Calculate ongoing requirements **over 48 hours**
 - Give both **over 48 hours** – serum sodium should not fall faster than 0.5 mmol/hr
 - If oral rehydration, replacement is over 24 hours
 - Diabetic ketoacidosis:
 - If give insulin too fast, serum glucose will drop quickly \rightarrow rapid change in ECF osmolality \rightarrow cerebral oedema
 - If giving hypotonic solution then \uparrow cerebral oedema – go slow
 - Rehydration of **hyponatraemic** dehydration (serum Na < 130):
 - Resulting from gut or renal losses, or excessive hypotonic fluid administration
 - Appear more dehydrated than they are as fluid shifts into the ICF. Can \rightarrow cerebral oedema, seizures, etc
 - Never give 1/5th normal saline (except to keep vein open). Do serial Na measurements
 - If asymptomatic: As for rehydration of isotonic dehydration, over 24 hours. Fluid restrict to 50% of maintenance
 - If symptomatic (seizures, coma) or if severe (Na < 120) then give 5 – 10 ml/kg or 3% hypertonic saline IV over 60 – 120 minutes in addition to the calculated fluid requirements
- Notes:
 - Be careful about measuring volume: never hang a bag straight into a child
 - If lung or brain disease (eg meningitis), SIADH is common \Rightarrow may need to fluid restrict (eg to 50% maintenance fluids). Check serum Na regularly
 - In a term baby, born water logged (ECF > ICF). Can pass 500 ml urine per day (7 ml/kg/hour). Handles water well but not used to passing a NaCl load
 - Enemas for constipation can \rightarrow dehydration

Paediatric Coma

- Assessment: Coma scales – main function is to assess progress
 - AVPU scales
 - Glasgow scale (but designed for adults)
 - Child Coma scale
- General observation:
 - Alert states:
 - Fully alert (what this mean depends on age of child)
 - Confused
 - Delirium: agitated and confused
 - Reduced alertness:
 - Lethargic: fails to maintain wakefulness without stimulation
 - Obtunded: drifts into sleep unless constantly woken
 - Stuporose: unconscious but withdraws to painful stimuli

- Comatose: fails to respond. May be decorticate or decerebrate. At risk of airway failing
- Differential in children:
 - Hypoxic: respiratory or circulatory failure
 - Epileptic seizures
 - Trauma: intracranial haemorrhage, brain swelling
 - Infections: meningitis, encephalitis
 - Poisons
 - Metabolic: Renal, hepatic failure, Reye's syndrome, hypoglycaemia, diabetes, hypothermia, hypercapnea
 - Vascular lesions: bleeding, AV malformations, arterial or venous thrombosis
 - Hypertension
- Diagnosis:
 - Must be bilateral cortex or brainstem involvement
 - Is it focal, multifocal or diffuse
 - Is it getting better or worse
 - Metabolic disturbances (including hypoxia and seizures) account for 90% of unconscious children
 - Supratentorial mass lesions compressing the brain stem: 3rd nerve palsy and dilated pupil on same side – NOT 6th nerve palsy
 - Subtentorial lesions affecting the brain stem directly: slow pulse, high BP, irregular breathing
- Management:
 - Stabilise vital functions: ABC then DEFG
 - Complete history: esp trauma, poisoning, previous diseases – diabetes, epilepsy
 - Exam: vital signs and progression, trauma, neck stiffness, CNS function, and:
 - Verbal responsiveness
 - Ocular responses: eye opening, papillary responses and spontaneous eye movement, ocular reflexes (eg Dolls eye)
 - Respiratory patterns: Cheyne Stokes (rate slows down, stops, restarts), irregular, apnoeas, stridor
 - Motor system: Motor responses, reflexes, tone, posture
 - Investigations:
 - Blood: gases, electrolytes, glucose, FBC, LFT, ammonia, calcium, lactate, clotting factors
 - Urine: poisons, sugar, organic acids, ketones
 - Chest Xray, consider skeletal survey
 - ECG
 - CT Scan
 - LP only when safe: risk factors – prolonged fits, focal neuro signs, purpuric rash, CGS < 13, dilated pupils, reduced Dolls Eye, abnormal posture, signs of herniation, coagulation disorder, papilloedema, hypertension

Paediatric Trauma

- Most common cause of death < 14 years (way out in front)
- Under 1 year: cause of death – congenital abnormalities > infection > trauma
- Trauma: poisoning > suffocation > MVA
- What makes kids different:
 - Large, poorly supported head. Always land head first
 - Thin skin → ↑ evaporative skin losses and burn at a lower temperature
 - ↑ Surface area: mass ration → ↑ rate of heat loss
 - Relatively large, poorly attached spleen
 - Renal function, conserves water, secretes sodium
 - Greenstick fractures
 - Child abuse: differential diagnosis in all cases of trauma (do history and physical findings correlate)
- Dealing with children:
 - Never lie – say if it's going to hurt
 - Kid that is injured will almost always have been injured doing something they were told not to do – child will consider you part of the punishment
 - Parents will get mad at you because they feel guilty. Wear it – this is not the time to deal with it
 - Child will regress

- See When is a child really sick?, page 565

Resuscitation

- Summary:
 - A. and cervical spine
 - B.C.
 - Exsanguinating haemorrhage (if it's not bleeding, ignore it)
- Get help early
- **Airway and cervical spine** immobilisation: Look/listen/feel
 - Airway opening: Jaw thrust
 - Suction of foreign material *under direct vision*
 - Airway devices:
 - Oropharyngeal/nasopharyngeal airways, ET tube, surgical airways.
 - Oropharyngeal: Right size: should reach from midline of lips to angle of the jaw. Use tongue depressor to help insert oropharyngeal (cf adult)
- **Breathing:**
 - Monitor:
 - Work of breathing: rate, noises, recession, accessory use, grunting
 - Effectiveness of breathing: breath sounds, chest expansion, SpO₂
 - If inadequate commence assisted ventilation
 - Indications for intubation:
 - Inadequate O₂ via bag mask
 - Inability to protect airway (eg do they have gag reflex, muscle tone in jaw, etc)
 - Prolonged ventilation required, or control required (eg in transport)
 - Flail chest
 - Inhalational burn injury
 - Intubating
 - If using sedating drugs, must be confident you can completely manage ventilation, do surgical airway if necessary, etc
 - Pre-oxygenate if possible with high flow O₂
 - Need: working, correctly sized laryngoscope, suction, bag valve mask, syringe
 - Take collar off to intubate
 - Tube size = (age/4) + 4 (or size of kids little finger)
 - Must secure tube or it will slide out
 - Auscultate the chest to check air entry and check end-tidal CO₂
 - Identify and treat life-threatening problems:
 - Tension pneumothorax: ↓sounds on affected side, trachea shifts to good side → needle decompression in 2nd intercostal space, midclavicular line, then chest drain. Little harm if they don't have a pneumothorax.
 - Open pneumothorax: 3 sided sealed dressing then chest drain
 - Massive haemothorax: chest drain and cardiothoracic consult
 - Flail chest: intubate and ventilate. Rare in kids as ribs too spongy – but can get very severe injury without breaking ribs
 - Cardiac tamponade: Urgent cardiothoracic consult
- **Circulation:**
 - Assess: heart rate, pulse volume, central capillary refill < 2 secs (eg over sternum after 5 secs pressure), skin temperature
 - Identify and treat life threatening problems:
 - Shock
 - Stop uncontrolled haemorrhage
 - Stabilise pelvis
 - Initial management of shock:
 - O₂
 - Large IV line placement. If can't then inter-osseous needle. 1 cm medial and distal to tibial tuberosity. Have to squeeze in fluid
 - Crystallloid 20 mls/kg bolus. Reassess and repeat if needed. After that, warmed blood. After transfusion of > ½ blood volume then FPP.
 - If still unstable consider blood and urgent surgical opinion

- Keep them warm
- **Disability** (ie simplified coma scale):
 - A: Alert
 - V: Responds to voice
 - P: Response to pain
 - U: unresponsive
 - Pupils and posture (decorticate/decerebrate)
- **Exposure:**
 - Uncover to inspect for injuries
 - Keep warm and minimise embarrassment
- **Glucose:** all severely injured children at risk of hypoglycaemia: check during primary survey
- **Assessment:**
 - Monitors: Pulse/BP/RR/SpO₂/Temperature + EtCO₂ if intubated
 - History taking: parents/ambulance crew/child, past medical history, medications, allergies, last meal
 - Blood tests: baseline FBC and U&Es, cross matching, glucose
 - X-rays: Trauma series – AP chest, AP pelvis, lateral C-spine. NB Soft bones are less likely to break despite strong force \Rightarrow ↑ chance of internal organ damage in absence of breaks than in an adult (eg ribs)
 - Urinary catheterisation/naso-gastric tube placement
 - Analgesia: morphine, 0.1 – 0.2 mg/kg IV (*not IM*)
 - NG tube to empty stomach: kids graze all day so stomach never empty. Also, swallow lots of gas when in pain \rightarrow tube lets air out \rightarrow ↓risk of aspiration due to pressure in stomach and less pressure on thorax
 -
- Then secondary survey: head to toe inspection

Traumatic Injury

- Head injury almost never causes shock
- Frequency of visceral injury: spleen > liver > kidney
- Splenectomy. The younger the child the greater the risk of fatal post-splenectomy sepsis (adults have greater previous antigenic exposure so less susceptible). Leave it in if vital signs stable
- Kidney trauma: most common injury is contusion \rightarrow mild haematuria
- Bladder: easily ruptured
- Closed head injury:
 - Full neuro exam
 - Level of consciousness: **A**wake, responds to **V**oice, to **P**ain, or is **U**nresponsive
 - Localising signs: can be very subtle, watch for changes
 - Pupils
 - Can rupture middle-meningeal artery without fracturing skull
- Pain management: early – consider regional blocks (eg femoral nerve block in fractured femur)

Car crash

- Without seat belt, risk of death is ↑10 times. All children being held in the front seat die
- Assessment of severity:
 - Speed of crash
 - Was seatbelt on
 - Was child thrown from car
 - Was any other child killed

Burns

- > 50 % of burn admissions are children
- Full thickness burns don't hurt (nerves are dead)
- Partial thickness burns blister and heal
- Rule of 9's doesn't work – needs age adjustment
- Fluid resuscitation: Ringer's 4ml/kg/% of burn (half in 1st 8 hours) + maintenance (ie pour it in till they urinate)

Paediatric Anaesthetics

Pre-operative assessment of child with a URTI

- Peri-operative risk variably increased
- Postpone high risk:
 - Neonates and infants
 - Existing upper airway/respiratory pathology (eg CF) - ↓ reserve – easy to tip over the edge
 - Systemic symptoms
 - Lower respiratory tract involvement
 - Surgical impact on respiratory function (eg upper abdo surgery)
- Complications usually manageable

Pre-operative assessment of child with a murmur

- Innocent murmurs often detected by anaesthetists
- Murmurs in up to 95%, but pathology in only 0.5%. May need referral for investigation
- 3 Common innocent murmurs:
 - Early systolic from ventricular outflow tracts (either pulmonary or aortic)
 - Continuous murmur from SVC
 - Grade 1 – 2
- Bad murmurs mimicking benign ones:
 - Severe hypertrophic obstructive cardiomyopathy
 - Critical aortic stenosis
 - These develop after birth – so may not have been picked up in post natal checks
- Postpone and refer if suspicious, esp if < 1 year
- ECG recommended if echo unavailable (can fax to a paediatric cardiologist for interpretation)
- SBE prophylaxis may be indicated

Risk Factors for Aspiration

- High risk for aspiration: Treat as full stomach
 - Full stomach
 - Regurgitation
 - Impaired protective reflexes
 - Airway obstruction (big negative pressure in thorax in order to suck air in past obstruction – but this also sucks contents out of stomach)
- Hazards of fasting:
 - Discomfort
 - Hypovolaemia. Guidelines are:
 - Clear fluids till 2 hours before
 - Breast milk till 4 hours before
 - Food till 6 hours before (no chewing gum)
 - Hypoglycaemia: only an issue for neonates

Assessment for Sedation

- Need to risk assess any child before any sort of sedation – its all too easy for something to go wrong (or more usually, for lots of little things to mount up)
- Always need to be confident you could ventilate, intubate and get IV access quickly if necessary

Pain Management in Children

- Myths:
 - Neonates don't experience pain
 - Neonates have no memory of pain (they retract from a needle the 2nd time)
 - Pain is not harmful (it leads to stress response → ↓healing, etc. ? Impact on the development of pain pathways)
 - It is dangerous to treat pain
- Management principles:
 - Mild to moderate pain relief is achieved through oral or rectal doses
 - Children hate needles, especially repeated IM injections
 - Using loading doses and regular maintenance doses to achieve therapeutic effect
 - Don't overdose with paracetamol (may → hepatotoxicity). Limit duration

- Child-friendly environment and parental involvement important
- Available drugs:
 - Paracetamol (oral better than rectal). Only use aspirin where specially indicated (eg Rheumatic fever)
 - NSAIDs: Diclofenac, Ibuprofen, Naproxen
 - Codeine Phosphate (metabolised to morphine): constipation, plus dose related opioid side-effects – sedation, respiratory depression, nausea and vomiting
 - Morphine for serious pain (eg burns and fractures)
 - Pethidine less used in kids - ↑ toxicity (including seizures)
 - Tramadol – not often used but less respiratory depression
 - Nitrous Oxide (always administered with O₂). OK for brief analgesia (eg fracture immobilisation). Ensure resuscitation equipment available. Mouth pieces preferred to masks

Child Abuse

Central elements in maltreatment

- Parent's strong negative and irrational engagement with the child, featuring a distorted perception of the child
- Parent's lack of ability to engage positively with the child
- Child is continually left in a state of worry or anxiety

General History

- History of injuries – how, who, when, where. Note details of different caregivers, change over times, etc. Clarify custody arrangements well
- Developmental history
- PMH, especially previous injuries (do you need notes from hospital, other GPs etc)
- Social history: supports, domestic violence, other stresses, previous CYFS referral
- What are parent's expectations of toddler behaviour, etc

Physical Abuse

- Non-accidental injury to a child or young person
- Includes: bruises, cuts, fractures, head injuries, injuries to internal organs, suffocation, poisoning, burns
- Risk factors:
 - Hard to parent child: eg handicapped or behaviourally difficult
 - Poor parenting skills/experience
 - Unrealistic expectations of the child
 - Poor mental health of the parents
 - Reduced social support
 - Alcohol or substance abuse
 - Domestic violence
 - History of child abuse in the abuser
 - Triggering event precipitating loss of control by the perpetrator
- Be suspicious when:
 - No history is given for the injury
 - The history changes
 - History is partial
 - Unbelievable explanation
 - Unreasonable delay in seeking help
 - Previous similar episodes
 - Parents' affect or behaviour is abnormal
- Questions to include in history taking:
 - When, where and how did the injury occur
 - What was the child doing at the time
 - Who saw it
 - What is the child's developmental level
 - Is a scene examination necessary
- Patterns of injury suggesting non-accidental injury:

- Fractures: multiple sites or different ages, rib fractures, any fracture in a child < 2: consult radiologist. Look for missing teeth
- Head injuries: any child < 1, unexplained coma, retinal haemorrhages (from shaking). Usually closed head injury rather than a fracture
- Bruises: on face or back, non-mobile baby, fingertip pattern bruises, other pattern bruises (strap, belt), yellowing \Rightarrow older than 18 hours. If suspicious, referral immediately to a paediatrician (who can arrange for evidential photos to be taken). Tell mum you need to refer so they can be checked for other injuries
- Burns: Child will withdraw hand or foot before a burn is full thickness, pattern burns (eg held in hot bath, cigarette burns), burns on back
- Examination:
 - Normal general assessment: growth, consciousness, play and behaviour, language
 - Carefully full survey: looking for bruises, tenderness, acute abdomen (eg splenic rupture), genital bleeding (leave full genital exam for an expert)
 - Developmental assessment
 - Systems Review – any other possible cause for the injuries
 - Document everything carefully, use a body chart and measure lesions, ask for explanation of each injury
- Investigations:
 - FBC and coagulation
 - Referral for specific investigations: X-ray, ophthalmologist, ENT surgeon, CT
 - Consider urine toxicology
- Differential to physical abuse:
 - Bruising: Mongolian spots, coagulopathies, coin rubbing
 - Cigarette burns: bites or vesicles
 - Hot fluid burns may be non-intentional
 - Fractures: osteogenesis imperfecta, spiral fractures of the tibia in toddlers

Sexual Abuse

- Any act resulting in sexual exploitation of a child – whether consensual or not, including:
 - Non-contact abuse: exhibitionism, suggestive behaviours, exposure to pornography
 - Contact abuse: fondling, masturbation, oral sex, object or penis penetration
- Risk factors:
 - Family dysfunction
 - Female sex
 - Pre-adolescence
 - Previous victimisation: don't think they're worth it – won't say no
 - Non-biological parent
 - Developmental delay: don't understand, scarred to say no
- Alleged perpetrators are all ages. If < 10 years, are they acting out abuse to them. 60% are family members
- History taking:
 - Evidential interview is the job of the police and CYPFS – usually videoed
 - If child discloses to a doctor, record questions and answers carefully. Don't ask leading questions. Qualify notes with "the above history was taken in order to direct the exam and does not necessarily constitute a full or detailed history". If not acute, leave questions for police
- Presentation:
 - Behavioural indicators: non-specific so don't over interpret. They're the same for anything that's upset them, eg parents separating: sleep disturbance, change in appetite, regression, running away, fear (specific or generalise), anger, \downarrow concentration, sexualised behaviour
 - Adolescence: self-harm, suicidal ideation, alcohol/drug abuse, eating disorders, unprotected consensual sex, promiscuity, school failure, loss of peer group
 - Vaginal discharge in a pre-pubertal child is common:
 - Non-specific eg irritant/allergic
 - Infection: Gp A strep, shigella, Candida (uncommon once out of nappies)
 - Foreign bodies
 - Polyps
 - Systemic illness eg measles, chickenpox
 - Vulvar skin disease

- Vaginal bleeding: accidental straddle injury, vaginitis, foreign body, precocious puberty
- Normal sexual development:
 - 0 – 2: genital exploration, masturbation (boys > girls), learning names
 - 3: talk about sexual differences, genital interest increases, masturbation common
 - 4: Play doctors and nurses, mothers and fathers, games involving undressing, exhibitionist activities, demand privacy for themselves, interested in others bodies
 - 5 – 6 years: familiar with and has less interest in sexual differences, likely to be more modest
 - Sexualised behaviour:
 - Masturbation is normal, but inappropriate if older and still public
 - Sexual play: if > 5 shouldn't be touching other genitals
- Physical findings in abuse:
 - > 50 % of disclosures will have no physical findings
 - Urgent forensic exam only if incident < 72 hours ago
 - Perpetrator usually doesn't want to hurt the victim, otherwise won't have continued access ⇒ physical injuries less common
- Investigations:
 - Pre-pubertal: don't screen for STD's unless symptomatic. HIV testing in time if high risk
 - Adolescents: screen for STDs and ?pregnancy test
- Prognosis: 25% have no adverse psychological sequelae. The more invasive the abuse, the more severe the effects long term

Neglect

- = Act or omission that results in impaired physical functioning or development, or injury. Includes physical neglect, neglectful supervision, medical neglect, abandonment, refusal to assume parental responsibility
- Risk factors:
 - Poor attachment
 - Parental psychiatric illness
 - Maternal depression
 - Isolated unsupported parent
 - Poverty
- Presentation:
 - Often associated with physical and emotional abuse
 - In an infant: failure to thrive, frequent attendance at A&E, severe nappy rash, unexplained bruising, cold injury, developmental delay, attachment disorder
 - Pre-schoolers: short stature, unkempt and dirty, delayed language, very disorganised play (eg aggressive and impulsive, indiscriminate friendliness)
 - School children: short stature, poor hygiene (including teeth), unkempt, learning difficulties, ↓self esteem, disordered/few relationships, unusually patterns of defecation or urination

Emotional Abuse

- = Act or omission that impairs the psychological, social, intellectual or emotional development of a child or young person. Includes: Rejection, isolation, oppression, deprivation of affection, inappropriate criticism, threats or humiliation, exposure to violence, involvement in illegal or anti-social activities, negative impact of substance abuse or mental/emotional condition of parent or caregiver
- Risk factors:
 - Poor attachment
 - Parental psychiatric illness
 - Maternal depression
 - Isolated unsupported parent
 - Parental alcohol and/or drug addiction
 - Domestic violence
- Presentation:
 - Socio-emotional indicators: can't enjoy themselves, refuses to defend self, cheats, steals, bizarre or extreme behaviours, failure to accept responsibility for behaviour, low self-esteem, withdrawal, defiance, compulsivity, seeks love and acceptance outside the home, apathy
 - Cognitive indicators: learning problems, short attention span, hypervigilance, hyperactivity, developmental delay, lack of curiosity

- Physical indicators: Failure to thrive, accident prone, self destructive behaviour, eating disorders, GI and bowel problems, poor posture, sleep disorders, ↓energy
- Differential: Munchausen's by proxy

Management of Abuse

- Paramount principle: The interests, safety and well being of the child should be the paramount concern (Section 6, Children, Young Persons and Their Families Act)
- Doctor's role is medical management, not the assessment of child abuse
- If child abuse is suspected:
 - Trust your instincts
 - Look for signs of abuse
 - Document the facts
 - Recognise and treat medical sequelae
 - Prevent pregnancy
 - Provide ongoing support, and watch for and help behavioural sequelae
 - Contact CYPFS immediately and discuss your concerns. You cannot be guaranteed anonymity, but when reporting to CYPFS or the police you are protected from court action if acting in good faith
 - Mother/other person can also contact CYPS [good approach if you consider this is really a custody issue. Alternatively advise the mother to get a lawyer]
 - There is no legal requirement to contact CYPFS or to give a CYPFS social worker information if they contact you. There is likely to be an ethical obligation, and referral guidelines will exist and should be followed.
- Investigation and management is multi-disciplinary: should involve paediatrician, social worker, police, psychologist
- If a child discloses abuse:
 - Listen to the child but do **not** interview them
 - Well being of the child comes before the interests of any other person
 - Write down what the child says
 - Reassure them they've done the right thing
 - Tell them that they will get help – but don't make promises. Say it's got to stop but that you'll need to tell someone else who will help
 - Tell your manager/supervisor as soon as possible
 - Look after yourself: discuss the matter with someone you trust
 - If nothing seems to be happening, contact CYPFS again
 - Complete an ACC M45 form and forward to the Sensitive Claims Unit at ACC
- Care for mother: may be domestic violence, depression, addiction, etc
- Care for perpetrator: talk with intake social worker about help for them (eg violence prevention programmes)

Mental Health

Attention Deficit/Hyperactivity Disorder (ADHD)

- Background:
 - Estimates range from 2 – 5%
 - Boys > girls
 - 60% take some symptoms into adulthood (eg restless, disorganised, poor attention, impulse control)
 - Was first described 100 years ago – only recently received appropriate recognition
 - Could be better described as ‘behaviour inhibition disorder’
 - Is strongly genetic and is biological
- Diagnosis:
 - Behaviour:
 - Inattention: easily distracted, doesn't finish tasks, works best with supervision, poor short-term memory. “How does he get on with daily tasks like dressing/eating breakfast/doing homework” “Do you ever have to stand over him to make sure he finishes”
 - Impulsiveness: acts without thinking, short fuse, aggressive, little self-control. “How often does he get into trouble for not thinking before he does something”

- Overactivity: restless, fidgets. “How easy is it for him to sit still”
- Insatiability: rarely satisfied, interrogates, over-intrudes in others space
- Also poor co-ordination, disorganisation, fluctuation, and specific learning disabilities
- Older child: low self esteem, mood swings, aggression, underachievement
- Inappropriate for age and development
- Pervasive across at least 2 settings
- Onset < 7 years
- Impairs social and academic functioning
- Hard to diagnose pre-school – tantrums and ↓attention common. Issue is whether they mature on transition to school. Gap widens as they get older. A 6 year old should be able to complete tasks, concentrate, etc
- Usually normal to high IQ
- Diagnostic boundary is disputed – this falls on a continuum (like everything else!)
- Differential:
 - Learning disability → not coping at school, frustrated → acting out
 - Gifted child whose bored
 - Psychosocial stress: disruption at home, abuse
 - Anxiety
 - Psychiatric disorders (mood, anxiety or personality)
 - Problems with parenting – no boundaries or inconsistent boundaries
- Associated factors:
 - Lower socio-economic status: poverty, poor housing, unemployment, illness, family breakdown
 - Childhood depression/anxiety → ↓concentration
 - Auditory/visual perceptual difficulties → inattention, loose interest
 - Reading problems: visual sequencing, letter-word orientation → appears inattentive
- Assessment:
 - Onset of behaviours
 - Situation specific or pervasive
 - Other learning difficulties
 - Context: parents management style, life events, teacher, etc
 - Use parent questionnaire
 - What are child's strengths – basis of self esteem
 - Get information from school: general behaviour, problems in specific situations (transitions between lessons, unstructured time eg playground, changes to routines eg outings, academic problems)
 - Thorough developmental history (ABFWIMPS), especially:
 - Head injury
 - Perinatal problems
 - Attachment problems in first 2 years (eg PND, stresses, violence, drugs)
 - Exam: dysmorphic features, tics (more common in ADHD and also side effect of ADHD medication), observation during interview
- Classifications:
 - Primary: early onset, feeding/sleeping problems from early on, overactive/unmanageable toddler, parents exhausted
 - Secondary:
 - Psychosocial causes: family disruption, demands of school, etc
 - Specific learning disability (→ ↑stress once school starts)
 - Mixed: an adolescent presenting with all of the above, plus ↓self-esteem
- Management:
 - Multidisciplinary assessment
 - Behaviour strategies:
 - Clear, firm, consistent guidelines
 - Check understanding of instructions
 - Anticipate problems and have planned responses ready → ↓parental stress and ↑consistency
 - Avoid triggers (eg crowds)
 - Predictable routines (eg at bedtime)
 - Managed use of time out, withdrawal of privileges
 - Encouragement: see Behaviour Management, page 570

- At school:
 - Structured approach – plan day
 - Sit near teacher, between quieter kids
 - Brief, clear instructions
 - Supervision during transition times (coming in from breaks, etc)
- At home:
 - Force leads to confrontation, resentment, broken relationships
 - Behavioural techniques work poorly – it's a biological problem
 - Ignore all but the important misbehaviours. Have a few clear rules, with clear consequences, if broken act without argument. Don't debate or escalate
- Esteem: Encourage. Find something they are good at. Swimming, bike riding, cooking, judo and computers may be better than team sports. Encourage friendships – take a friend on outings
- Diet: < 10% sensitive to synthetic food colouring
- Many dodgy therapies: avoid unless proven
- Stimulant medication:
 - → Concentrate for longer (stimulates inhibition) → complete tasks → less disruptive and ↑ self-esteem
 - First: education for child and parents.
 - “Have you heard about medication – what?”
 - Address myths: they're addictive, they sedate the child, child at ↑risk of substance abuse later in life
 - Side effects: sleep disturbance, appetite suppression (small effect, if marked → growth suppression), moodiness, rebound, tics
 - First line options are Methylphenidate (Ritalin) or Dexamphetamine. Both require specialist endorsement. Introduce slowly. Short T½ ⇒ need to fine tune dose times. Eg give before school → Ok at school but difficult by the time they get home. Not in evening otherwise ↓sleep. Review – should have noticeable improvement, if not re-evaluate
- Referral if:
 - Diagnosis/differential in doubt
 - Assistance with management of challenging behaviour
 - Assessment of role of family relationships in perpetuating the problems

Anxiety Disorders

- See also Anxiety Disorders, page 422
- Fears are normal during childhood and adolescence:
 - Age 1 – 2: fear of separation from parents
 - Young child: scared of the dark, animals, storms, monsters
 - Age 7 – 8: begin to worry about their performance
 - Adolescents: concern about being disliked, rejected, or criticised by their peers
 - ⇒ Fears generally reflect developmental stage
- Anxiety disorder:
 - Fears become intense or pervasive and substantially impair functioning
 - Can follow chronic, fluctuating course
 - Not easy to recognise as young people often know that their fears are groundless and feel ashamed of what they think is a flaw in their character
- Anxiety disorders: Separation anxiety disorder, social phobia, generalised anxiety disorder, obsessive compulsive disorder, post-traumatic stress disorder

Separation Anxiety Disorder

- Child very anxious away from home or from their parents
- May present with:
 - Refusal to attend school – but school's not the problem, the separation is
 - Feeling physically ill in the morning. Monday's the worst day
 - Reluctance to sleep at friends places, school camps, etc
 - Worried that harm will befall their parents while they're away
 - Difficulty coping with parents going out
 - Difficulty going off to sleep, or needing company of a parent while they do
- History should include:

- School: problems, bullying, fears, etc
- Home: stressors, conflicts
- Maternal depression, anxiety, adjustment disorder, etc
- Parents may have some insight – but usually underestimate the severity of the maternal-child dependence and are very defensive
- Diagnosis: irrational fear of harm to parents or that they will be abandoned by them
- Differential for school non-attendance:
 - Truancy, conduct disorder: doesn't go to school – but doesn't stay at home either
 - Anxiety-based refusal
 - Major depression: lacks motivation
 - Other reasons: at home to help with work, etc
- Epidemiology: F > M. Peaks in early adolescence
- Course:
 - May be triggered by a worrying or traumatic incident. May be family history of anxiety problems
 - Eventually become isolated from friends and get behind at school. Feel embarrassed and different.
↓Self esteem. All makes returning to school more difficult
 - Prognosis depends on the young person, family strengths and severity
 - Increased risk of agoraphobia in adulthood
- Management:
 - Support for parents and child
 - Quick return to school before problem becomes entrenched, even if only for a small portion of the day
 - Education for child and parent. Facing the fear is initially distressing but reduces the anxiety, avoidance increases it
 - Parents need to be consistent in their commitment to return the child to school
 - Involve school teachers (eg meet at gate, etc). Problem is actual separation – once settled into the day problem is likely to reduce
 - Severe or chronic → referral. Support for parents if they're having difficulties. SES Behaviour Support Teams or Resource Teachers for Learning and Behaviour (RTLBs) for child.
 - No place for medication unless underlying conditions

Bullying

- = An act of aggression/harassment by a child/youth
- Starts mid-primary, peaks 3rd form, nearly gone by 7th form
- Typical bullying behaviour: boys hit, girls tease and exclude
- Teachers generally under-estimate bullying
- Characteristics of someone who is bullied:
 - Something different: high achiever, less physically attractive, etc
 - Vulnerable: more anxious, cry easily, don't fight back
- Problem compounded for the bullied in that no one wants to be friends with a person who is bullied → ↑isolation. Standing up to a bully is pretty sophisticated behaviour in early teens – not developmentally consistent with wanting to identify with the peer group
- Long term outcomes worse for the bully than for the bullied

Depression

- See also Mood Disorders, page 426
- Mood disorders are prevalent and serious disorders in children and adolescents. Leads to difficulties at school and in social relationships
- 1 year prevalence estimated as high as 10%
- Same diagnostic criteria as for adult – but diagnosis harder. More likely to present with separation anxiety, phobias, somatic complaints and behaviour issues. More likely to talk of profound boredom and feeling unloved and lonely than appetite and sleep change
- Most do recover, but recurrence is more common than in adults
- Clinical approach:
 - See the teen on their own
 - Observe: ↓energy, anxiety, anger, shame, variability in affect
 - Listen: the teen is more likely to talk if they feel they are being heard
 - Consider differentials: Depression, drug abuse, eating disorder, psychosis (actual or prodrome), medical

- Suicide assessment
- Aetiological factors to consider:
 - Family context
 - Cultural context: are they comfortable about who they are in a cultural sense
 - Peer group: Have they friends, how do they support him/her?
 - School: bullying, what's hard at school, current stressors
 - Life events: losses, abuse
 - Psychological: negative ways of thinking, learned helplessness
- Treatment involves the child, parents and school. Aim is to shorten the episode. Treatment can include:
 - Education
 - Counselling: for milder depression, no remediable family factors, recent life events, if they want it
 - Family therapy
 - A range of individual therapy types – usually through referral
 - Medication: less evidence of effectiveness in adolescents. Consider discussion with a psychiatrist. Usually SSRIs
- Referral when:
 - Significant suicide risk
 - Possible psychosis
 - Abuse
 - Severe family discord
 - Failure to improve

Youth Suicide

- See also Suicide Assessment and Management, page 416
- Epidemiology:
 - Second only to MVA as cause of death – but still uncommon.
 - 3 fold rise in last 30 years.
 - Females attempt, males succeed
 - Second highest rate for 15-24, Finland higher
- Postulated factors contributing to increase:
 - ↑Depression and substance abuse
 - Unemployment
 - ↑Isolation and alienation
- Key issue: identifying those at risk
- Risk factors:
 - Male gender
 - Psychiatric illness: depression (most common association), alcohol or substance abuse, personality disorder, psychosis
 - Previous suicide attempts
 - Available means: firearms, toxic medications
 - Social adversity: recent interpersonal loss, homelessness, school failure or drop-out, family or relationship problems, unemployment
 - Recent exposure to suicide
- Most common presentations are over-dose, self-poisoning and lacerations
- Management:
 - Treat underlying psychiatric disorder (not TCAs – too lethal in overdose. Use SSRIs)
 - Reduce ongoing stress: counselling to reduce interpersonal conflict
 - Promote social supports
 - Liaise with specialist health services

Other Mental Health Issues

- Eating disorders: See Eating Disorders, page 453
- Substance Abuse:
 - Drug and alcohol use prevalent
 - Often comorbidity

- Sexual maturation: sexual behaviours, orientation, attitudes to sex and relationships, awareness of socially defined roles. Knowledge about pregnancy and STIs doesn't automatically translate into behaviours
- Risk taking behaviour:
 - Adolescence is a time of experimentation, pushing boundaries
 - Contributing factors: ignorance, impulsiveness, cognitive immaturity (sense of omnipotence and poor comprehension of long term consequences), peer groups, drugs and alcohol

Adolescent Health

Definition of Adolescence

- Developmental period between childhood and adulthood
- Age of majority in NZ = 20 years
- WHO definitions:
 - Adolescents: 10 – 19
 - Youth: 15 – 24
 - 10 – 24: Young people

Demographics

- Young people are the only age group whose health status has not improved in the last 40 years
- Current issues:
 - Accidents and injuries
 - Mental health issues
 - Health risk behaviours: smoking, alcohol, drugs, sex
 - Chronic illness: eg obesity, asthma, diabetes, etc
- Access to health services for adolescents fragmented – fall between child and adult services

Adolescent Development

- Summary:
 - An age of transition
 - Experimentation and change: inherent risk taking
 - Behaviours reflect maturational tasks
 - May use maladaptive behaviours to achieve developmental goals (eg smoking to gain peer acceptance). Need to change them to adaptive behaviours
- Also see Cognitive Development, page 578
- Physiological:
 - Puberty: highly variable – generally from 9 – 14 years. Can take 2 – 5 years to complete
 - Gain 25 cm in height, 50% of ideal adult body weight
- Stages of adolescence:
 - Early: coming to terms with body/biological changes
 - Middle: establishing self among peers as a worthwhile individual
 - Late: vocational/education direction and one-to-one intimate relationships
- Developmental issues
 - Abstract reasoning
 - Preoccupied with their own thinking
 - Peer group membership and conformity important
 - Consolidation of self image and identity
- Psychosocial:
 - Who am I and where do I fit in
 - Identity: self, culture, ethnicity, sexuality
 - Autonomy vs relatedness/connectedness
 - Goals and future direction
- Developmental tasks of adolescence:

Tasks	Early: 10 – 13 years	Mid: 14 – 16 years	Late: 17 – 21 years
Psychological tasks			
Independence	Separates from parents: questions, tests	Separation creates anxieties, ambivalence as retreats to family	Comfortable away from home, able to return for counsel

Body image	Adjust to dramatic changes in body Constant comparisons	Try on images to find real self (incl. Sexual identify), attempts to improve image	without shame Satisfied with realistic body image
Sexual drives	Marked sexual curiosity, masturbation	Sexual experimentation, narcissistic sexual relationships	Beginnings of intimacy and caring
<i>Social Tasks</i>			
Relationships	Boys 'gangs', girls 'best friends'. Crushes on adults	Other sex friendships, dating, try on other philosophies and beliefs	Individual relationships more important than group, ↑ intensity of relationships
Career plans	Vague, unrealistic	↑ Efforts but influenced by 'escape' from home, glamourousness of career	Hard decisions → occupational identity. Delayed by higher education
<i>Cognition</i>	Concrete, literal, limited abstraction	Formal operations; use abstractions (what if...), introspection, less literal	Mature abstractions, problem-solving & self-reflection
Moral Growth: values	Need to follow rules of peer group or family	Narcissistic: feels good or is what I want ⇒ right → impulsiveness	Idealism, rigid standards of right and wrong, intolerance

Talking with Adolescents

- Keys to effective intervention:
 - A positive relationship
 - Thorough assessment
 - Inclusive of family and young person
 - Plans made with the young person and family
- Building a trusting relationship: introductions
 - Friendly, confident welcome but still professional
 - Introduce yourself directly to the teen, 'And is this your mum?'
 - Clear introductions: yourself, your role, what you'll be doing and why
 - Clear boundaries: explain that you see young people alone and with family and why:
 - 'You're on your way to being an adult. Want to support that process. But your parents also still have a role'
 - Allows them both to say things they might not in front of the other
 - Outline confidentiality:
 - 'I want to talk about confidentiality. Do you know what that means?.... Want to keep your information private'
 - 'There are 3 things I can't keep a secret: if someone's harming you, if you're harming yourself or if you're harming someone else. I need to do something about it – but will tell you what I'm doing'
 - 'Will talk to my colleagues for review – to check I'm doing the best I can'
 - Consider what you put in notes (they get around). Use standardised abbreviations.
 - If adolescent doesn't want you to tell parents (and you think it's in adolescents best interests for them to know):
 - Why doesn't teen want parents to know ('You seem worried about your parents knowing this. Can you tell me about that?')
 - Attempt to persuade the teen to tell her parents
 - Offer to tell them yourself
- Keys to building the relationship:
 - Be keen to get to know this young person now
 - Accepting atmosphere
 - Respect
 - Non-threatening explanations
 - Give adolescent some control – encourage normal independence

- Reveal hidden agendas
- Give them time to talk – hold off asking questions
- Make plans with the young person and family
- If they don't want to talk, probably anxious/frightened. “It seems you're pretty angry about being here. Did someone make you come?”
- Communication:
 - Use language that is understood (no medical or adult jargon). *Check understanding*
 - Listen
 - Move from less sensitive to more sensitive topics
 - Move from third person approach to the personal
- Set clear boundaries: It is appropriate to identify what is and is not acceptable behaviour (eg creating risk of harm to themselves or others). Middle adolescents still require the security of clear boundaries. However, try not to be judgemental
- Beware:
 - Transference: person projects their feelings about someone else (eg parents) onto you
 - Counter-transference: You transfer feelings appropriate to someone else (eg your own kids) onto the adolescent (eg act as though you were their parent)
 - Objectivity: understand the most likely reason they won't talk is that they're frightened

HEADSS Risk Assessment

- Gives an overview of this individuals risk and resiliency
- If you don't ask they won't tell you
- Do ask, even if you think you know the answer
- **Home:**
 - Where do you live and whom do you live with?
 - Who do you get on with, who would you talk to if you had a problem?
 - What's good about home? What's not so good?
 - Who makes the rules and what happens if they're broken?
 - Is there ever any violence at home?
- **Education/Employment:**
 - What do you enjoy most about school?
 - What subjects do you like?
 - How are you getting on at school?
 - Do you get into any trouble?
 - How do you get on with your teachers/friends
- **Activities:**
 - What do you do after school/in the weekends?
 - What do your mates do? (Get an idea of peer relationships)
 - What did you do last weekend that you enjoyed?
- **Drugs:**
 - ‘I check with all young people – not picking on you. Remember it's confidential. You don't have to answer if you don't want to’
 - Lot's of people your age smoke/take drugs/drink. Is it like that at your school?
 - What do you think about that?
 - What have your friends tried? What about you?
 - If no, make it positive ‘that's fantastic - how come you don't and lots of others do?’
- **Sexuality:**
 - Most young people have become interested in sex at your age. Have you had sex education at school? What was it about – body changes, infection, preventing pregnancy, relationships?
 - Do you talk with anyone in your family about sex
 - Have you had a sexual relationship with anyone?
 - Do you have sexual feelings to boys or girls? Ever had sexual experiences with someone your own sex? If this is confusing or frightening for them then need to talk further.
 - Want to help you stay healthy...ask about safe sex
 - If not active – encourage them. But also check they can get condoms, etc: ‘if you ever were to, where would you go for information or contraceptives (tie them down to specifics)
- **Suicide risk and Depression:**
 - ‘Everyone has good days and bad days. Do you ever have really good days? Really bad days?’

- ‘Often adolescents see me because they’ve been feeling down. How have you been?’
- ‘Have you been happy with the way things are going? How would you rate yourself over the last couple of weeks if 1 was foul and 10 was brilliant?’
- ‘Do you ever feel like you want to end it all?’
- ‘Do you have a plan to hurt/kill yourself?’
- ‘How do you plan to?’
- Determining the degree of risk:
 - Well adjusted
 - Vulnerable
 - Experimenter
 - Troubled
 - Out of control
- See Youth Suicide, page 663

Physical Exam

- Use chaperones
- Be thorough but assure privacy and modesty (work around clothing)
- Talk and explain (especially about growing bodies)
- Pubertal ratings: Get them to self report genital development off an Adelaide chart – don’t examine yourself unless specific problem

Puberty

- Physiology:
 - Pre-puberty: Inhibition of GnRH pulse generator by higher centres
 - Puberty: increasing frequency and amplitude of pulsatile GnRH secretion, initially at night, with FSH (\rightarrow follicles or Sertoli cells) and LH (\rightarrow hormone production) secretion in response
 - Also involvement of adrenal glands \rightarrow androgens \rightarrow secondary sex characteristics (eg pubic hair but not \uparrow testicular size)
- Terminology:
 - Gonadarche: onset of gonadal function
 - Thelarche: onset of breast development
 - Adrenarche /Pubarche: Onset of development of sexual (pubic/axillary) hair
 - Menarche: Onset of menstruation
 - Spermarche: Onset of production spermatozoa
- Clinical signs:
 - Measured in Tanner stages (1 = no development, 5 = adult)
 - Girls: breast development first (ovaries enlarge first but can’t see them)
 - Boys: Testicular enlargement (use orchidometer)
 - Pubic hair development initially related to adrenal androgens and may be discordant with other changes
- What’s normal:
 - Girls: traditionally < 8 years or > 13 years abnormal. But \uparrow number of girls have breast development at 7. Menarche relatively unchanged at 12 (ie earlier onset, but endpoint relatively unchanged). Getting earlier by 3-4 months per decade (but psycho-social development unchanged)
 - Boys: < 9 or > 14 abnormal. No strong evidence of it getting younger

Normal variants

- Mini-puberty in neonatal period
 - Usually neonate – but up to 4 months
 - Due to hormones in utero and underdeveloped CNS inhibitory mechanisms
 - Breast development +/- milk (Witches milk - completely normal)
 - Withdrawal uterine bleeding (following endometrial development in utero)
 - Estrogenic effects on genitalia
- Premature Thelarche
 - Isolated early breast development
 - Tanner 2 or 3 maximum
 - No advancement in bone age
 - Follow-up to ensure it is isolated not progressive (ie that it’s a normal variant)
- Premature Adrenarche:

- Isolated early pubic hair development +/- acne +/- BO
- Caused by adrenal androgens
- No advancement in bone age and normal menarche/spermarche
- Need follow-up (eg to exclude adrenal tumour)
- ?Association with future hyperandrogenism (eg Polycystic Ovary Syndrome)
- Gynaecomastia:
 - Breast development up to stage 3 during male puberty (75% of males)
 - Usually in early puberty – resolves in about 2 years
 - Reassurance, occasionally surgery
 - Pathological:
 - In rare instances: Klinefelter's syndrome, gonadal failure
 - Outside of puberty (eg oestrogen producing tumour)
- Key sign indicating normal: normal bone age/no growth spurt

Precocious Puberty

- Definition arbitrary
- Consequences:
 - Short stature
 - Psychosocial (out of sync with peers)
- Clinical signs: Old bone age and growth spurt (in addition to eg breast development)
- Gonadotrophin Dependent:
 - = Central/complete. Hypothalamic or pituitary cause and → balanced development
 - Girls:
 - Normal progression through puberty (ie variant of normal?)
 - Rapid progression suggests pathology
 - Boys:
 - Normal progression of puberty
 - Less common than girls, more likely to be pathology
 - Causes:
 - Idiopathic (95% in girls)
 - Hypothalamic hamartoma: developmental anomaly
 - Tumours (eg of hypothalamus or pituitary)
 - Other CNS conditions (eg hydrocephalus, spina bifida)
- Gonadotrophin Independent:
 - = Peripheral/Incomplete. Peripheral cause and not all characteristics of normal puberty
 - Girls: rapid progression or virilisation
 - Boys: Testes remain small, rapid progression
 - Causes:
 - Hormone ingestion
 - Congenital Adrenal Hyperplasia (ie adrenal androgens)
 - Tumours: adrenal, gonadal or hCG secreting
 - Autonomous hormone production (rare)
- Investigations:
 - Bone age from hand x-ray
 - Measure hormones
 - GnRH stimulation test
 - Imaging
- Treatment:
 - GnRH agonist for central precocious puberty via depot. If GnRH is not pulsatile it switches off FSH and LH
 - Girls: progesterone delays menarche

Delayed Puberty

- Hypogonadotropic: Hypothalamic/pituitary causes:
 - Constitutional delay (check for bone age)
 - Exercise/nutrition (eg anorexia)
 - Generalised pituitary failure (eg post surgery/radiotherapy for CNS tumour)
 - Rare isolated deficiencies

- Hypergonadotrophic: Gonadal failure
 - Chromosomal: eg XO, XXY
 - Infections (eg mumps, especially during puberty)
 - Autoimmune
 - Surgery, radiotherapy, chemotherapy
 - Galactosaemia
- Other:
 - Structural (eg normal puberty but no menarche)
 - Intersex disorders: chromosomal sex <> phenotypic sex
- Pubertal arrest: always pathological (eg pituitary tumour)
- Investigation and treatment:
 - Gonadotrophins +/- GnRH stimulation test
 - Hormone replacement
 - Fertility issues (eg with gonadal failure)

Chronic illness and disability in Adolescents

- See also Effect of Chronic Disease on Development, page 582
- Between 1- 20 % of young people have a chronic or disabling condition
- US prevalence:
 - Asthma: 50/1,000
 - Mental retardation: 25/1,000
 - Epilepsy: 4.1/1,000
 - Diabetes mellitus: 4.1/1,000
 - Down syndrome: 1.1/1,000
 - Cystic fibrosis: 0.2/1,000
- Survival rates are improving
- Developmental impacts:
 - Primary: effects of the disease
 - Secondary: effects of delayed development
 - Tertiary: effects of treatment
- Similar risk taking behaviours to healthy adolescents
- Impacts on development:
 - Most don't have major problems, and consider their illness less severe than doctors do
 - Process of separation from parents may be slowed if dependent on parents for care or limited opportunities to socialise with peers
 - Learning disorders → embarrassment, failure, frustration, ↓self worth, performance anxiety, learned helplessness
 - Slowed sexual development or physical deformity → problems with sexual identity
 - Normal developmental issues such as struggle for independence, concrete thinking, narcissism (what feels good is right) and sense of omnipotence (future is a long way off) → non-compliance with treatment
- Mental health in those with chronic illness:
 - Highly variable
 - Vulnerable periods: early years, transitions, severe illness
 - Important variables: onset, disruption to early attachments, premorbid function, family stress, mental health of parents, experience of failure or victimisation, repeat hospitalisation, life expectancy
- Resilience:
 - Focus on the young person not just the disability/illness
 - Focus on building strengths, achieving successes
 - Competence in self-care/management of illness/disability
 - Access to age appropriate coping strategies
 - Opportunities for responsibility/required helpfulness
 - Family relationships
 - Peer relationships
 - School attendance

Health Care of the Elderly

- References: Medicine in the Older Adult, Dr Mark Weatherall, Wellington School of Medicine

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History

- History should include:
 - Function of the person before their illness
 - Current function of the person
 - Their aims and aspirations:
 - Where do they anticipate living on discharge from hospital
 - What functional level must they achieve for this to happen
 - Has the availability, ability and opinions of carers and family been taken into account
 - Are there special social or cultural considerations
 - Are the goals of the person and the family reasonable within a realistic timeframe
 - Has there been sufficient consultation
 - What is the physical layout of the home, access to and within it
 - Screen for disorders

Assessment of Functional State

- Include the following in the social history
- Basic activities of daily living:
 - Mobility: can they move in bed, get in and out of bed, in and out of a chair, on and off a toilet, ability to get around the house, to get outside, to get to the shops or visit friends. Can steps and stairs be managed
 - Urinary & Faecal Continence: is there a problem, how is it managed
 - Bathing, shaving, teeth, dressing: how much assistance is needed, can they reach all body parts
 - Feeding: how much assistance is needed (eg cutting up food)
- Advanced activities:
 - Handling of finances
 - Shopping
 - Use of public transport
 - Preparation of a hot drink

Screen for Disorders

- Cognitive impairment: delirium, dementia, focal cognitive impairments (dysphasia, non-dominant hemisphere problems). May need to use an assessment instrument (eg mini-mental state) and/or interview others
- Visual and hearing impairment
- Postural hypotension
- Malnutrition
- Faecal impaction
- Pressure areas
- Iatrogenic disease, including adverse drug reactions
- Weakness secondary to immobility
- Untreated or under-treated pain

Residential Care History

- Reasons for living in a residential care facility, how long have they lived there
- Past health problems and current concerns
- Current medical treatment
- Current functional state
- Social network (family and other visitors), and interests and activities
- General physical examination
- Screen for common impairments
- Formulate a problem list, and management strategies (including preventative) that may be appropriate

Ageing

- = Net effect of age related changes → ↑likelihood of dying
- Age related changes affect all body systems: cardiac, respiratory, CNS, musculoskeletal, vision, hearing, skin, immune and renal

- Demographics:
 - ↑ In absolute number of 60, and > 60s as a proportion of total population

	Number > 65	% of total population
1976	275,000	8.9%
1996	423,000	11.7%
2016	659,000	15.5%
- Life expectancy at birth for NZ females is 79.5 years and for males 74.3 years (3rd to lowest in OECD)

Concepts

- Cohort Effect: Each current age group (eg adults now aged 80 – 90) have experienced a distinctive history, leading to the following cohort effects:
 - Disease and disability with roots in environmental exposure varies from cohort to cohort (eg tobacco use, diet, peak bone mass)
 - Cross sectional studies should consider cohort effect (eg medical care available to 80 year olds when they were 30, compared with 30 year olds now). A difference may not be due solely to aging
 - Cultural and social differences between cohorts: eg response to health professionals, access to services, gender and spiritual issues
- Diversity of physiology and function increases with age: stereotypes are unhelpful, need individual assessment
- Multiple pathology: Not a single disease process presenting acutely, but a person presenting with disease(s) and/or disabilities. Need a model of care and assessment that considers individual disease processes, individual experience, the social context, and interactions between and within these dimensions
- Failure to present (professionals need to initiate strategies to overcome):
 - Self stereotyping: I'm just old, there's nothing they can do, etc
 - Cognitive impairment and depression
 - Disability: eg ↓ mobility
- Atypical presentation: Strange or unusual presentations are more common compared with younger people, due to multiple diseases, reduced homeostatic capability, etc. Can be non-specific (not coping, immobile, etc)
- Threshold effect: Change in functional status can occur in the absence of a clear precipitant due to build up of subclinical dysfunction and loss of physiologic reserve
- Disordered homeostasis and the cascade effect: Age related effects → ↓ ability to maintain homeostasis in the presence of a threat (eg medication). Disordered homeostasis in one system can trigger dysfunction in another
- Caring for carers is important in maintaining people in the environment of their choice

Disability

- Disability is understood by (WHO definition):
 - Pathology: abnormal structure or function of an organ or system. Eg osteoarthritis
 - Impairment: Loss or abnormality of psychological, anatomical or physiological function. In decreasing order of prevalence in the elderly these are (in a CHCH study): visual impairment, hypertension, symptomatic spinal osteoporosis, hearing impairment, stroke/TIA, osteoarthritis of the hip or knee, urinary incontinence, dementia, postural hypotension
 - Disability: Any restriction or lack of ability to perform a task or activity. Eg for elderly women in Mosgiel: housekeeping, shopping, bathing, mobility
 - Handicap: disadvantage for a particular individual resulting from impairment or disability that limits fulfilment of a role normal for someone of that age, culture, gender, etc. Eg reading a newspaper, shopping, etc
 - However, some things don't fit well into this model (eg psychiatric illness). WHO currently revising. Will also include impact of environment (eg not being able to drive is not always a disability – eg if you live in the 3rd world)
- Interventions should address all levels, and acknowledge the interaction between each level
- Reported disability has a clear age associated increase

Age Related Problems

- For Osteoporosis and Osteoarthritis, see Metabolic Bone Disease, page 261

- For Postural Hypotension see Measuring Blood Pressure, page 19
- For Congestive Heart Failure see Heart Failure, page 48
- For Hypertension see Hypertension, page 34
- For Alcohol Withdrawal see Alcohol Withdrawal, page 452
- For Delirium and Dementia, see Dementia, page 439
- For Urinary Incontinence, see Urinary Incontinence, page 223
- For Constipation see Constipation, page 177
- For Pressure Ulcers see Pressure Ulcers, page 327
- For Pharmacology and Age see Age, page 526
- For Stroke see Stroke, page 125
- For Hearing Impairment see Presbycusis, page 151
- For Insomnia, see Sleep, page 534

Iatrogenic Disease

- Hospitalisation is dangerous to older people, especially leading to: drug toxicity, injury and mental deterioration
- There is often a decline in functional status following discharge, unrelated to disease process
- Elderly have ↑susceptibility to variety of stressors
- Bed rest (eg in hospital, especially if on drips, monitors etc) generally leads to ↓outcomes, due to:
 - ↓Muscle strength and aerobic activity
 - Volume depletion therapy (also results from bed rest) + age related vasomotor instability → postural hypotension
 - Supine position worsens V/Q mismatch
 - Bone demineralisation
 - ↑Urinary incontinence due to high beds or distance from toilet
 - Pressure sores
 - Sensory deprivation (eg boring rooms, not wearing glasses or hearing aids)
 - ↓Nutrition (altered dietary habits, unappetising food, ↓social component to eating)
 - All lead to a cascade of interaction
- Most deterioration happens in first two days in hospital. Examples of prevention include:
 - Low bed without rails
 - Carpeting
 - Minimisation of tethers
 - Encouragement and assistance
 - Orientate with clocks, calendars, dressing, undressing, communal dining
 - Sensory stimulation: proper lighting, decoration, glasses, hearing aids, available recreation

Nutrition

- Can be measured through body weight (eg BMI), body composition, or direct measurement of micro-nutrients
- Under-nutrition in the elderly can be due to:
 - Age related ↓ in gastro-intestinal function predisposes to poor nutrition (eg ↓teeth, ↓pancreatic secretion, etc)
 - Life-style factors: inability to shop, prepare and cook food, living alone, alcohol abuse, poverty
 - Diseases: eg stroke, arthritis, dementia make eating harder
 - Anorexic effect of illness and drugs
- Management:
 - Multidisciplinary: dietitian to advise on what and how much to eat. Occupational therapist to advise on food preparation. Meals on wheels. Social worker to involve family and ensure adequate finance
 - Medication review
 - Nutritional supplements: eg add milk powder to food, eat high-density foods, take supplements

Falls

- In elderly, refers to a fall during an activity that is usually safe
- 25 – 35% of those over 65 fall each year. Occurrence ↑ with age
- < 5% of falls cause a fracture (40% of these to proximal femur). Soft tissue injury in 40%
- Staying upright (a homeostatic function) requires:

- Safe environment
- Information on body position: visual, vestibular, mechanoreceptors, proprioception, central processing
- Motor systems: cortex, brainstem, cerebellar, spinal chord, muscles
- Stable base: joints, limbs, feet
- Intact judgement
- Causes of falls:
 - ‘Threshold model’ in which a number of factors combine to ↑risk
 - Sedative use, cognitive impairment, abnormalities of balance and gait, polypharmacy, history of stroke, hypotension
 - Fall over things that are safe to others ⇒ changing the person more important than changing the environment. But check for rugs, clutter, cords. In hospital, care with ability to transfer, agitation and frequent toileting
- Associated diseases:
 - Nervous system: stroke, Parkinson’s, dementia, seizure, peripheral neuropathy, ↓visual acuity
 - Musculoskeletal: proximal muscle weakness, arthritis of lower extremity
 - Cardiac: aortic stenosis, arrhythmia, postural hypotension
 - Iatrogenic: sedatives, psychotropic medication, alcohol
- Assessment:
 - Previous history of falls
 - When, where, what was experienced, associated environmental factors
 - History of vertigo, dizziness, imbalance, blackouts, medication
 - Examination: postural changes in BP, vision and hearing
 - Observation: stand up without using hands, observe gait, stop smoothly, turn around, stand with eyes closed, stand on one leg, reach up, bend over, heel toe walking, can they speed up, nudge them, sit down without hands
- Management:
 - Active management of injuries: watch for occult pelvic fractures, hypothermia. Care with soft tissue wounds – can easily go on to ulcers
 - Acute precipitating illness that requires treating: eg stroke, MI
 - Identification of risk factors
 - Rehabilitation: active mobilisation after a fall. Interventions targeted at identified risk factors, including medical review of medication, physiotherapy for transfer skills and exercise program
 - Avoid giving psychotropic medication to people at risk; it WILL make them fall over

Visual Impairment

- Major causes of ↓visual acuity in adults are (See also Loss of Vision, page 141):
 - Cataract: due to ↑bulk of the lens and discolouration. Age, diabetes, and UV light are the main risk factors. Treatment by extraction and implantation improves visual acuity in about 90% but a smaller proportion benefit in terms of activities of daily living
 - Age related macular degeneration: Variety of causes. More serious ones include choroidal neovascularisation → detachment and scarring
 - Glaucoma
 - Diabetic neuropathy
- Senile arcus: ring of lipid and calcium salts in a ring at the junction of the cornea and sclera. Very common in elderly. Not a sign of hyperlipidaemia (as it is in the young)
- Ectropion: low lid falls away and tears don’t drain into lacrimal sac
- Lens becomes thicker and less flexible (Presbyopia) ⇒ can’t accommodate, need reading glasses

Elder Abuse

- = When a person aged over 65 experiences harmful physical, psychological, sexual, material or social effects caused by the behaviour of another person with whom they have a relationship implying trust (Age Concern definition)
- Elder abuse can be:
 - Physical: physical pain, injury, force, under/over medication
 - Psychological: causing emotional anguish or fear, including intimidation, humiliation, harassment, threats, removal of decision making powers
 - Sexual
 - Financial: improper use of funds or other resources

- Can be:
 - Active neglect: conscious deprivation by a carer of basic necessities
 - Passive neglect: refusal/failure of a carer to provide the basic necessities due to inadequate knowledge, infirmity, or dispute over the value of services
- Prevalence: Significant under-reporting due to cognitive impairment, fear, life long pattern of abuse, access to someone to complain to, stigma associated with domestic violence. ?About 5% of elderly people subject to abuse, usually by a spouse, child or relative
- Risk factors for abuse:
 - Dependence by the older person for all or part of their care
 - Cognitive impairment, especially disruptive or aggressive behaviour
 - Substance abuse or mental illness of the abuser
 - Shared living arrangements
 - External stress
 - Social isolation
 - History of violence
- Screening for elder abuse:
 - Will not be volunteered: need to ask the right questions
 - Watch for injuries or health or emotional problems with vague or inconsistent explanations
 - Observe interactions, especially in own environment
 - Question older person away from carer:
 - Do you feel safe at home?
 - Are you afraid of anyone at home?
 - Have you ever been hit or pushed?
 - Question carer in empathetic not confrontational way: Caring for X must be difficult... How do you cope.... Have you ever lost control?
 - Careful physical examination and documentation of findings
- Management:
 - Age Concern have people trained in the assessment of abuse, plus case workers and advisory groups
 - Use ATR social workers
 - If person accepts intervention, then initiate a safety plan
 - If person declines intervention (but has the capacity to do so) then educate and review
 - If person declines but doesn't have the capacity to make this judgement, then family court can decide on welfare guardianship through the Protection of Personal and Property Rights Act (PPPR Act)

Driving

- 50% of 76 – 80 year olds still have a licence, 27% of those over 80. Half still drive regularly
- Driving depends on cognitive function, motor function and sensori-perceptual function
- Elderly are only 14% of those killed in crashes, but have a higher death to injury ratio
- Older drivers more likely to be at fault in accidents involving intersections, merging and manoeuvring
- In elderly people with Alzheimer's, crash rates approach those of 15 – 25 year old males
- Age associated changes affecting driving include: vision, psychomotor function, strength and dexterity, cognitive function (especially attention to multiple stimuli and finding ones way, ↓ in dementia)
- Medical assessment a legal requirement at 75, then 80 and every two years thereafter (including vision check). Cognitive screening should be included due to the profound effect on driving, the insidious nature of cognitive impairment, good social facades by patients, and frequent lack of insight.
- Psychoactive drugs (especially BDZs) → ↓ psychomotor function
- Practical test performed by the Ministry of Transport is required at 80 and every two years thereafter

Services for the Elderly

Rehabilitation

- Can classify approaches to rehabilitation by patterns of disability:
 - Localised injury or isolated disability: involvement of one discipline may be appropriate
 - Expectation of return to premorbid function: but more than one discipline necessary (eg fractures)
 - Where optimal recovery depends on well integrated team approach (eg amputation, stroke)

- Progressive deteriorating conditions where the aim is to maintain optimum ability, with regular review of goals, and emphasis on emotional, social and environmental factors rather than specific rehabilitation techniques (eg Parkinson's)
- Can classify rehabilitation by types of people:
 - Impaired physical function, but not obviously ill → disability management
 - Chronic illness without manifest disability → education and anticipatory care
 - Those with a combination of illness and disability
- Can classify rehabilitation by approaches:
 - Medical: specific control of disease and impairment
 - Prevention: Of secondary disability (eg pressure areas, constipation)
 - Restoration: Using physiotherapy, occupational therapy and nursing interventions to ↑ function
 - Adaptation: Equipment, modification of living environment, and family adjustment
- Also need to assess the strengths and abilities of the individual and carers
- Goal Setting:
 - Central task in management of disability
 - Needs accurate assessment of pre-morbid and current function (eg using formal assessment tools). Is often unrealistic to aim for future function better than pre-morbid function
 - Goals must be meaningful and appropriate to the problems and circumstances
 - Goals should be agreed by negotiation with older person, the carer and the rehab team
 - Goals should include: who, will do what, under what circumstances, and to what degree of success
- Barriers to Rehabilitation:
 - Unidentified medical problems: don't want to over *or* under-medicate. Check for malnutrition, anaemia, fluid and electrolyte abnormalities
 - Cognitive impairment: If they can't concentrate or remember, their involvement is compromised. Always screen for impairment
 - Depression: Unwell and disabled people have a high prevalence of usually treatable depression. Diagnosis can be complicated due to overlapping symptoms (eg fatigue, apathy, psychomotor retardation and sleep disturbance)
 - Communication problems: Screen for poor eyesight and hearing
 - Low expectations and ageism: decline is not always as inevitable or severe as thought. Patients, carers and professionals can all have misconceptions and unrealistically low expectations
 - Right to dependency: some old people may not participate because they feel they should be looked after
- Common rehabilitation interventions: physiotherapy (especially musculo-skeletal problems and mobility), occupational therapy (therapy to ↑function in tasks, ↓impairment), doctors (diagnosis, prescribing, prognosis, co-ordination), nursing (implementing therapies, assessing disease, function and well being), speech language therapy (including swallowing), dieticians, appliances, adaptations, daily living aids, advice, education, counselling, encouragement, listening
- Whether inpatient or outpatient setting is assessed on the basis of: level of dependency (especially night care), degree of complexity of disability, speed of response needed, housing and domestic circumstances, availability of in or outpatient services

Rest Home and Hospital Care

- 6% of the population over 65 live in institutions (about 25,000), 24.5% of those over 85
- Rest homes are licensed by the Ministry of Health and payments are made by the Ministry of Health
- Access to funding by an individual is dependent on a needs assessment done by an HHS or other assessment unit and an asset test done under contract from the Ministry of Health by WINZ
- Maximum weekly fee paid is \$636: average rest home fees are around \$550 per week and hospital fees around \$1100
- If receiving the subsidy, you loose super and get an allowance of \$27 per week
- Needs assessment assigns a Support Need Level (SNL) from 1, little help needed, to 5, 2 person help needed – levels 1 and 2 general aren't funded to be in rest homes
- Comorbidity common in rest homes, plus evidence of mental illness (in addition to stroke and dementia)
- Other health issues include vitamin D supplementation, immunisation (including of staff), and loss of continuity of care on shifting into a rest home
- Also broader issues are maintenance of privacy, whether sexual needs can be met, encouragement of health promotion activities such as exercise, appropriate recreation, monitoring dietary intake, provision of alcohol and attitudes to smoking

Public Health

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Introduction

- WHO Definition of Health: A state of complete physical, mental and social well being, not just the absence of disease or infirmity
- Public Health:
 - = The art and science of preventing disease, prolonging life and promoting health through the organised efforts of society
 - = Population health, not the public health system
- Roles of Public Health:
 - Traditional role: communicable disease control, environmental and occupational health
 - Information: disease and health surveillance
 - Policy: Policy, legislation, goals, priority setting
 - Health Services: planning, evaluation, needs assessment
 - Health promotion/disease prevention: promotion, screening, immunisation
- Steps in public health:
 - Public health intelligence (monitoring/analysis)
 - Developing policy
 - Delivering services
- Equity and access:
 - Need = capacity to benefit (but from whose perspective?)
 - Vertical verses horizontal equity (but equity of what – outcomes, access, opportunity)
 - Dimensions of affordability, accessibility, availability, acceptability, accommodation

Health Care Delivery

*Issues in Service delivery **

- Key international trends:
 - Changing demographics: esp ↑ elderly
 - Communicable → non-communicable diseases
 - Concern with economy given rising costs
 - Who should pay: public vs private
- Issues in service delivery:
 - Institutional arrangements:
 - Output funding
 - Priority setting
 - Funder/provider splits
 - Managed care
 - ‘Cultural’ issues:
 - Competition vs cooperation
 - Control vs community voice
 - Management vs technology
- Influences on NZ history:
 - 19th century legacy:
 - Parochialism (isolation → self-government)
 - Adhocracy (new problem → new organisation)
 - Egalitarian myth: services by right

System in NZ

- References: Introduction to the New Zealand Health System, Peter Crampton and Anne Viccars, Departments of Public Health and General Practice, Wellington School of Medicine
- Factors facing health systems in developed countries:
 - Ageing populations
 - Medical technology
 - Rising expectations
 - Treaty of Waitangi
- Health Care expenditure in New Zealand:
 - 1998 total: around \$8 billion. Vote health was \$5.6 billion in 97/98.

- 7.6% of GDP (compared with Australia 8.3% and UK 6.7%)
- Public 77%, private 23%.
- 18% of total government expenditure.
- Proportion of people covered by health insurance has declined since 1994/95
- Health Legislation:
 - Health and Disability Services Act 1993 (now repealed)
 - Health Act 1956: main piece of public health legislation
- Health Policy Agencies:
 - Ministry of Health
 - Other central agencies: Te Puni Kokiri, Treasury, State Services Commission
 - Other advisory bodies:
 - National Advisory Committee on Health and Disability (National Health Committee)
 - Mental Health Commission: established in 1986 following Mason Inquiry
 - Health and Disability Commission: established in 1994 – responsible for the Code of Health and Disability Consumers' Rights
 - Health Sponsorship Council: Established under smoke-free environments Act 1990 to sponsor activities previously sponsored by tobacco companies
- Purchasers: Used to be the HFA, including Pharmac and Health Benefits Limited
- Purchaser-Provider Split:
 - Potential benefits were:
 - Efficiency: due to competition
 - Equity: reflect need not historical provision
 - Accountability clearer
 - Cost containment due to capped budgets
 - Consumer sovereignty
 - Better information
 - Improvements in primary care: IPAs and Maori services
 - Problems:
 - Short term market lead decision making
 - CHE debt/missed business plans
 - Transaction costs → bad contracting relationships → 3rd party intervention
 - Asset specificity: providers locked in → little real competition
 - Fragmentation of services
 - Loss of co-operation
- Primary Care:
 - Numbers:
 - 2,800 GPs (about 2,500 FTEs)
 - 1,600 practice nurses
 - 1800 – 2000 practising midwives
 - Funding:
 - GP income derived from: Subsidies (depending on patient age and CSC/HUHC), patient fees, ACC
 - Primary Care Expenditure: 59% pharmaceuticals, GMS 15%, labs 13%, maternity benefit 8%
 - Themes: managed care, budget holding, integrated care
- Latest reforms:
 - Ministry of Health and HFA merged
 - 21 District Health Boards created (roughly around old Hospital and Health services): have a purchasing and a provision function
 - Maternity providers funded by MoH
 - DHBs fund NGOs, GPs, Private providers, public health providers
 - ACC continues direct purchasing from primary and secondary providers
 - Key changes:
 - No purchaser-provider split
 - Community control
 - Budget tension between primary and secondary services forced down from central agencies to DHBs
 - 21 Boards too many: diseconomies of scale

Measures of Health Status

- No single or ideal way of measuring a person's or a population's health status → wide range of tools
- Purposes of measuring health status:
 - Diagnostic: to discriminate between people with different health states
 - Prognostic: to predict future events
 - Evaluative: eg before and after a health intervention
- Measuring health status of individuals and populations:

Dimension of Health	Measures in Individuals	Measures in Populations
Mortality	Age at death	Life expectancy
Disability	Existence of a disability	Prevalence of a disability
Self-rated Health	Self-rated health	Average self-rating

Mortality

- Definitions:
 - Crude Mortality Rate: number of deaths per year for an entire population
 - Specific Mortality Rate: Number of deaths occurring within a subgroup of the population. Eg age, sex, or cause specific
 - Age adjusted mortality rate: adjusts with reference to a standard population to allow comparisons between populations with different age distributions
 - Premature mortality: death occurring before the average life expectancy within a given population
- Advantages:
 - Death is easy to diagnose
 - Is recorded, and doctors are legally bound to state the cause
- Disadvantages:
 - Cause not always accurately described
 - Reduces health status to being alive or not. Ignores the continuum of suffering and unhappiness

Life Expectancy

- = The expectation for life at birth for a population born in a specific year
- Calculation:
 - Period life expectancies: average life-time of a hypothetical group born in a specific year, assumes age and sex specific death rates won't change
 - Cohort life expectancy: follow through a real cohort until all are dead
- Making comparisons, eg between Australia and NZ:
 - Migration between the two countries
 - Ethnic groups (Maori, Pacific Islanders, Aborigines)
 - Socio-economic differences
- Potential years of life lost (PYLLs): potential years of life lost for a specific cause. Difference between age of death and the life expectancy at that age
- Changes over time have largely been due to social and economic changes (particularly public and personal hygiene). Contribution from health services is much less important

Morbidity

- = Incidence or prevalence of a condition or disease in a population over a set period of time
- Measurement:
 - 'Objective' measures:
 - Biochemical markers (eg blood glucose)
 - Physiological markers (eg blood pressure)
 - Pathological markers (eg tumour size)
 - Functional measures:
 - See also Disability, page 673
 - Impairment: reduction in physical or mental capacity – usually due to an organ/system. May be able to be corrected (eg reading glasses)
 - Disability: restriction in a person's ability to perform a certain task (eg walking)
 - Handicap: If disability limits ability to perform a normal role – depends on social context
 - Many measures assess degree to which people can undertake activities of daily living
- Sources of morbidity data: cancer registers, notifications (infectious diseases, workplace accidents), hospital discharges, GP registers

- Advantages: examines range of diseases beyond those that cause death
- Disadvantages:
 - Diagnosis can be ambiguous
 - Variation in recognition or reporting of disease

Self-reported or Self-rated Health Status

- More subjective
- Overlaps with health-related quality of life, encompassing physical health, psychological well-being, emotional well-being and social functioning
- For assessing Maori health need to incorporate relations with extended family and spirituality (obviously non-Maori are not spiritual and don't care about family!!)

Composite Measures of Health Status

- Independent Life Expectancy: average number of years living without disability. Equals life expectancy + prevalence of dependency. Ignores reversibility of some disabilities and transition from good to poor health
- Measures of the burden of disease:
 - Takes into account fatal and non-fatal outcomes
 - Disability Adjusted Life Years:
 - Estimate of years of healthy life lost
 - Similar to QALYs but standardised for use between populations and they also use age weights (lower weights in childhood and elderly)
 - Used to assess the burden associated with certain diseases or with particular risk factors (eg smoking)
 - In NZ, CV disease accounts for 24% of DALYS lost, followed by cancers and mental disorders
 - Criticisms:
 - Limited use to policy makers because they focus on health loss rather than potential gains
 - Don't take into account disability associated simply with old age
 - Requires extensive epidemiological data

Biostatistics

- Choosing study subjects:

Group	Specified by	Criteria
Target population	Clinical and demographic characteristics	Well suited to the research question
Accessible population	Temporal and geographic characteristics	Representative of the target population and easy to study
Intended sample	Sampling procedure	Representative of the accessible population and easy to do
Actual sample	Availability, and obtaining informed consent and required information	May or may not be still representative of accessible population

- Populations may be people, institutions, records or events
- Sampling frame is a complete list of individuals in the accessible population
- A sampling procedure is used to select a representative intended sample from the sample frame
- Avoiding systematic errors:
 - Trying to use sample mean to estimate the population mean
 - Statistic = parameter + bias + confounding bias + chance
 - Statistic: summary measure in a sample
 - Parameter: underlying value in the target population
 - Bias or Confounding → ↓internal validity
 - External validity is whether the study can be applied to the population I'm interested in – is it similar enough to the study population?
- Bias:
 - Bias = systematic deviation between the statistic and the parameter, due to defect in the design, conduct or interpretation
 - Occurs predominantly in design and data collection

- Selection bias: systematic error due to those who were selected and those who were not, so sample not representative of the defined population
- Information bias: a flaw in measurement exposures or outcomes that results in a differential quality of information between sub-groups/individuals.
 - Misclassification bias: Subjects erroneously categorised. If a random bias then ↓ association in results and odds ratio moves towards 1
 - Interviewer bias: systematic difference in soliciting, recording and interpreting of responses (↓ by training the interviewers – always check this has been done)
 - Recall bias: should be < 2 weeks for health events. Diet recall ~ 24 hours. If not random (eg case-control studies) then biased (eg if cases taken from records then there is variability in what was asked and recorded, versus uniform questionnaire for controls)
- Response bias: systematic error due to differences between those who volunteer and those who do not (eg bias from drop-outs and non-responders)
- See EBM Glossary, page 703, for further examples of bias
- Confounding bias:
 - A measure of the effect of an exposure on the risk of an outcome is distorted by an association of the exposure with other factors that influence the outcome
 - Standard ones: age, gender, ethnicity, socio-economic status, obesity, smoking, alcohol
 - As long as you collect data about the confounding factor, you can do something about it
 - Can control for confounding using matching, logistic regression or stratifying data
- Chance effect:
 - Standard error:
$$\text{standard error} = \frac{\text{standard deviation}}{\sqrt{\text{sample size}}}$$
 - Quantifies the precision with which the sample mean estimates the population mean
 - Says NOTHING about variability in the data
- Confidence interval:
 - Turns standard error into something we can interpret: sample mean +/- 1.96 * standard error
 - 95% sure the underlying value lies in the range
 - Width is dependent on:
 - Variation in observed data
 - The sample size (larger sample → narrower confidence interval → more precise estimate)
 - Degree of confidence we want
 - Accuracy depends on presence or absence of bias
- Tests of significance:
 - Tests of significance are a tool for statistical inference
 - Test compatibility of a set of data with the null-hypothesis: assume there is no difference between the means – what is the probability we would observe a difference as big by chance
 - P value: the probability of getting a value at least as extreme as the observed statistic. Threshold usually 0.05
 - Most common test statistics are chi-squared and t-statistic (compares two means). Both depend on degrees of freedom
- Power: = probability that the study will find a statistically significant difference if a true difference of a given size exists
- Data:
 - Qualitative: not numeric (eg hair colour)
 - Quantitative: can be continuous or discrete
 - Measurement scales can be nominal (categorical and unordered), ordinal (categorical and ordered) or interval (continuous)
 - Data description:
 - Categorical and discrete data: bar graphs, frequency distributions
 - Continuous data: histograms, frequency polygons
 - Central tendency: Mean or median (best measure of central tendency if skewed distribution)
 - Spread/variability: Standard deviation, percentiles or inter-quartile range
 - Correlation co-efficiency – degree of clustering around a straight line
 - If two variables are categorical and unordered then use relative risks and odds ratios

Epidemiology *

- Includes 2nd and 3rd year PDS notes
- = Study of distribution and determinants of health and disease in populations
- For Definitions of Risk and Odds Ratios, see Risks and Odds, page 703
- Bradford Hill Criteria for causation:
 - Time sequence: did the factor come before the disease – only necessary factor
 - Strength: large relative risks are seldom artefacts
 - Consistency: has an association been found elsewhere, using different methods?
 - Specificity
 - Dose-response relationship: does the risk ↑ with the level of exposure to the factor
 - Biological plausibility: is a causal risk consistent with current knowledge
 - Experiment: can an intervention study validate the result
- Summary of study types: (increasing power as you go down)
 - Descriptive (ecological) studies
 - Analytical (observational) studies:
 - Cross-sectional studies
 - Case-control studies
 - Cohort studies
 - Intervention (experimental) studies

Descriptive studies

- Personal characteristics (age, sex, occupation, social class, etc), place and time
- Measures of occurrence (⇒ descriptive):
 - Prevalence: Number with disease/Relevant population at a designated time
 - Incidence: Rate of development of a disease in a group over a period of time = number of new cases during a specific period/total at risk population
 - Need to compare for specific groups, or standardise for compositional differences in populations
 - Long duration illness → ↑ prevalence, short duration → ↓ prevalence
 - Incidence and prevalence are similar for short illnesses (eg diarrhoea) but not for long illnesses (eg TB)
- Useful for:
 - Understanding occurrence
 - Suggesting hypothesis – but correlation doesn't prove cause
 - Often called ecological studies
- Don't have unaffected people in the series so no information about relative risks

Cross-sectional studies

- Examine relationship between disease and other variables (eg risk factors) in a defined population at one time
- If prevalence not high enough, use sentinel populations (ie those with greater risk)
- Normally considering prevalence, not incidence ⇒ also called Prevalence Studies
- Limitation: time sequence of cause and effect cannot be determined

Case-control studies

- Factors amongst patients with a disease compared with the frequency among a control group without the disease
- Looking backwards to the exposure (ie the outcome has already happened) ⇒ also called retrospective studies
- Advantages:
 - Can be done quickly (compared with cohort study)
 - Are therefore cost effective
 - Can do it with diseases with low prevalence (cohort study better for more prevalent diseases)
 - Defined endpoint
- Disadvantages:
 - Retrospective, so can introduce bias
 - Selection criteria create difficulty
 - Biases: non-volunteer bias, recall bias, etc
 - Causation not proven – just an association

- Can only get information on one outcome
- Selection of cases:
 - Representative of those presenting over a defined period
 - Select according to diagnostic criteria. If these cast the net widely, then will include people with unrelated disease → odds ratio moves towards 1 (if random effect)
- Selection of controls:
 - Representative of the population from which cases drawn but without the outcome
 - Aim is to establish expected exposure in case group
 - Want to compare exposures between the cases and the population at large. If, for example, you match on age, you won't be able to conclude anything about age as a risk factor, so choose controls so you get an unbiased example of risk factors in the population. Matching does reduce the effect of confounding – but there are other ways to deal with that when doing the number crunching
- Identical methods must be used to collect information from both
- Can't estimate relative risk in a case-control study:

		Outcome (eg Disease)	
		Yes (Cases)	No (Controls)
Exposure	Yes	A	B
	No	C	D

- Odds Ratio = $(A/C)/(B/D)$
- Relative Risk
 - $= [A/(A+B)] / [C/(C+D)]$
 - = Risk of disease among exposed/risk of disease if not exposed
 - In a case-control study, the ratio between the cases and the controls is fixed by the study design, not the prevalence in the population. The relative risk is therefore meaningless. That is, you can't estimate the risk of the disease in the population in those not exposed to the risk factor
 - But if the condition is rare and there is no bias in controls, then the odds ratio approximates the relative risk ratio well
 - See also Risks and Odds, page 703

Cohort Studies

- Groups observed over time: forward looking from exposure, waiting for outcome ⇒ also called Prospective or Follow-up Studies
- Either compare within the cohort, or select a comparison cohort
- Advantages:
 - ↓Bias over a case-control study
 - Can examine more than one outcome
 - People who don't take part don't bias the outcome, just its generalisability
- Disadvantages:
 - Large numbers are required ⇒ information collected has to be simpler ⇒ ↑ risk of confounding
 - Need to follow people over time ⇒ expensive and takes a long time
 - Not good for rare diseases
- Strengths: People who don't take part don't bias the result – just affect its representativeness (ie external validity) ⇒ less susceptible to bias

Intervention or Experimental Studies

- Test whether removing suspected aetiological factors reduces frequency of disease
- Evaluate preventative measures and treatments (→ clinical and community trials)
- Best test of cause and effect
- Often not ethical nor logistical to do a RCT
- Blind assessment → ↓ information bias

Communicable Disease Control

- See Vaccination, page 515
- Reasons for notification:
 - High morbidity and mortality (in epidemiology terms, ie deaths per 100,000 of well population).
 - Intervention available
 - Other:

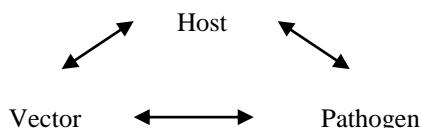
- High public interest. Eg CJD – is both rare and untreatable
 - Historical. Eg decompression sickness
- Notifiable Diseases:
 - Under Health Act 1956
 - Section A: infectious diseases notifiable to a medical officer of Health and Local Authority [involve water or food transmission]: acute gastro-enteritis (where common source or person in high risk occupation), cholera, giardiasis, legionellosis, primary amoebic meningoencephalitis, shigellosis, yersiniosis, campylobacteriosis, cryptosporidiosis, Hepatitis A, Listeriosis, salmonellosis, typhoid and paratyphoid fever
 - Section B: infectious diseases notifiable to Medical Officer of Health: AIDS, CJD, HIB, Hepatitis C, Hydatid disease, Leptospirosis, measles, Neisseria meningitidis, plague, rabies, rickettsial diseases, tetanus, yellow fever, anthrax, brucellosis, diphtheria, Hepatitis B, Leprosy, malaria, mumps, pertussis, poliomyelitis, rheumatic fever, rubella
 - Notifiable non-infectious diseases: cysticercosis, taeniasis, trichinosis, decompression sickness, lead poisoning, poisoning from contamination of the environment
 - All forms of TB (under TB Act 1948)
 - Venereal Diseases Act (1986?): covers gonorrhoea and syphilis, and contract tracing
- Classification of notifiable diseases:
 - Vaccine preventable diseases
 - Blood borne and sexually transmitted diseases
 - Food and water borne diseases
 - Vector borne eg Malaria
 - Zoonoses (ie animal stage) eg Brucellosis, Hydatids, Rabies
 - Other Infectious diseases: eg CJD, Hepatitis, Leprosy, TB
 - Non-infectious diseases: Decompression illness, Lead poisoning, environmental contamination
- Process of notification:
 - Is a legal requirement, although compliance is poor with common things like campylobacter. Only a small proportion contact doctor, only a few of these tested, only a few of these reported, etc
 - When to notify:
 - If serious on suspicion (eg meningitis)
 - If not serious (eg gastroenteritis) then on confirmation
- Possible interventions:
 - Food borne – isolate source and close it down
 - If AIDS and spread by blood products → screen blood
 - If AIDS and confined to a locality → education campaign
- Surveillance system:
 - Report to medical officer of health
 - Clinical labs also report to medical officer of health (if a special case then refer sample to the CDC Reference Lab – ESR).
 - These all report to the CDC Epidemiology Group (also at Porirua), produce the Public Health Report
 - In turn report to the Ministry of Health and MAF, so they can form surveillance and disease control policy (eg vaccination and screening policy, promotion, etc)
 - Other surveillance systems: coroner, Births, Deaths and Marriage, OSH, Cancer Registry
- Epidemics:
 - An outbreak or epidemic is relative, is ‘more than you would expect’
 - An outbreak investigation involves analysis of the *time* over which illnesses have occurred, the *places* and the characteristics of the *people* affected
 - Patterns of epidemic:
 - Point source out-break (eg food poisoning) – short duration
 - Multiple source out-break: eg measles, index case spreads to multiple cases – long duration with fluctuating incidence
 - Want to find:
 - Agent
 - Vector
 - Source
 - Can affect rate without known the agent. Eg cholera was controlled through clean water in London before the bug was discovered

Environmental Health

Classification

- = Effect of environment on health at a population level (want to stop people being sick...)
- Classify by route of exposure to agent of harm: Classify water, air and soil by physical, chemical and microbial (prion, virus, bacteria, protozoa, etc):
 - Water:
 - Physical
 - Drought
 - Drowning: in NZ have the hazard and lots of exposure (outdoor pursuits, fishing, swimming pools)
 - Microbial:
 - Virus: HAV, rotavirus
 - Bacterial: shigella, campylobacter
 - Protozoa: amoebae, Cryptosporidium, Giardia
 - Chemical: arsenic poisoning in Bangladesh
 - Air:
 - Physical:
 - Suffocation: plastic bags, volcanic gases, faulty gas appliances
 - High winds
 - Noise
 - Microbial: Tb, legionaries
 - Chemical: pesticides, asbestos, work place
 - Soil/Food:
 - Physical: landslide, earthquake, desertification
 - Microbial: tetanus
 - Chemical: heavy metals, selenium deficiency
 - Other: Sun (UVB → cancer), radiation
- Occupational health and psycho-social health often separated off from environmental health
- Need multi-disciplinary teams to solve problems (eg housing: doctors, engineers, sociologists, economists)

Inter-relationship of Host and Environment



Malaria

- Background:
 - Lifecycle: plasmodia in human blood → mosquito sucks blood → migrate into mosquito saliva glands → passed on in next bite
 - Host factors:
 - Sickle cell anaemia → ↓contagious
 - Immunocompromised: kids, malnourished, concurrent infection, maybe AIDS
 - Pathogen factors: which strain
 - Vector attributes: right species of mosquito
- Interventions:
 - Vector – Host relationship: Interrupt exposure eg nets, repellent, clothing
 - Host: general health, nutrition
 - Host – Pathogen relationship: chemoprophylaxis
 - Pathogen: Air-conditioning → ↓temp → ↓plasmodium
 - Pathogen – Vector relationship: Remove infected hosts (ie cure them)
 - Vector: source reduction (spray, ↓water traps)
- Effect of the environment:
 - Vector: if warm and wet breed faster
 - Host: if hot take clothes off and open windows

- Pathogen: plasmodium replicated faster if warmer
- See also Malaria, page 508

*Yellow Fever**

- Swotted for Public Health Test Question. Source: Harrison's and CDC Website
- Haemorrhagic fever with prominent hepatic necrosis
- Incidence declining since the turn of the century. Outbreaks mainly now only in West Africa. South America also at risk
- Urban Yellow Fever:
 - Spread by Aedes Aegypti mosquito
 - Human – mosquito – human cycle. Mosquitoes pass it to their offspring via ovary infection
 - Deposit eggs in any container with water in or around homes (so can still get it if low rainfall or dry season) ⇒ women and children more at risk if they're around home a lot
- Sylvatic Yellow Fever:
 - Mosquitoes infected from viraemic monkeys (monkey's don't get ill so are a continuing reservoir)
 - Infects humans in or living around forests ⇒ men who do the hunting more at risk
- Prevention (in addition to Malaria factors above):
 - Put bed nets over infected people – stops onward transmission of infected people. They are viraemic for 3 – 6 days, following a 3 – 6 day incubation period.
 - Treatment is supportive only. There is no chemoprophylaxis
 - Vaccination:
 - Safe, lasts for 10 years
 - Only vaccinate child < 12 months and pregnant women if high risk
 - Epidemics occur if poor maintenance of vaccination and lack of plans for detection and response to epidemics

Consequences of Global Environmental Changes

- ↑ Population:
 - Main driver of global changes
 - Carrying capacity of the world around 10 – 15 billion, currently 6 billion
 - Compounded by unequal distribution of resources: 20% have 80% of the resources
 - Technological change will only affect the 20% with resources ⇒ little impact on carrying capacity
 - Demographic transition: As countries shift from '3rd world' to '1st world' their pattern of disease shifts from infectious diseases with high infant mortality to degenerative diseases → The 80% will have ↑↑ resource requirements following this transition
- Global warming (due to ozone depletion, ↑CO₂, etc)
 - ↑ Vector born disease
 - Thermal expansion of oceans (melting ice caps comes later) + more frequent storms → flood low lying areas
- Resource depletion:
 - Wood, fossil fuels, food
 - Sources → resources used by people → sinks. If transfer is too fast, sources and sinks can't keep up
- Deforestation/desertification as a result of resource use and climate change
- War:
 - Due to competition for resources
 - Leads to all extremes of environmental health (death in combat, poor health, refugees, socio-economic effects)
- Trans-boundary population shifts (eg refugees)

Screening

Definitions

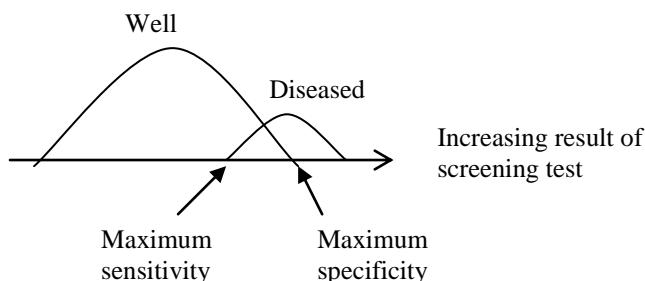
- Screening:
 - The presumptive identification of unrecognised/preclinical disease or defects by the application of tests, examinations or other processes that can be applied rapidly (and cheaply)
 - Sorts people into high and low risk groups for further diagnosis of high risk.
 - Is NOT diagnostic on its own

- Mass/population Screening: systematic screening of populations
- Opportunistic screening: Non-systematic, when the opportunity arises
- Selective Screening: systematic screening of high risk groups
- Screening test: a test performed without a clinical indication
- Objectives of screening:
 - ↓Mortality/morbidity from disease on the individual
 - Limit the impact of disease on a community
 - Identify compensatable disability (eg poor eyesight in kids)

Criteria for Screening Programmes

- Is the disease an important health problem (incidence, impact, preventability)
- Is a suitable screening test available:
 - Acceptable, simple,
 - High sensitivity, as specific as possible
 - PPV: probability that a person with a positive test does have the disease, depends on sensitivity, specificity AND prevalence
 - NPV: probability that a person with a negative test does not have the disease
 - Yield (proportion of cases of the disease accurately identified by a screening test),
 - Repeatability (depends on variation in method, subject variation, observer variation)
- Is the natural history of the disease well understood:
 - A recognisable latent or early symptomatic stage
 - The length of the asymptomatic stage determines screening frequency. Is this long enough to make the screening interval reasonable?
- Does screening lead to interventions that improve quality of life:
 - Does early intervention offer benefits over later intervention
 - Accepted treatment, proven effectiveness. Ideally want an RCT that demonstrate screening versus no screening improves mortality/morbidity
- Is there an appropriate infrastructure available to provide screening and follow-up services:
 - Are there pilot studies demonstrating how it should work?
 - Is there local and national support?
 - Are the services accessible (in terms of geographic, cultural barriers, cost), does the system have sufficient capacity, and is there appropriate quality control processes in place
- Is the screening programme cost effective?

Screening Test



- Eg PSA for prostate cancer, intra-ocular pressure for glaucoma, etc
- For a screening test, you want a test that maximises sensitivity: maximise true positives (minimises false negatives), so that you identify all diseased cases. The downside is an increasing rate of false positives who have unnecessary further investigation
- A highly specific test would maximise true negatives (ie minimise positives, so would not further test anyone unnecessarily), but at the cost of increasing false negatives – who are the people you actually want to detect
- See also Evaluation of Diagnostic Tests, page 704

Biases

- Lead-time bias: interval from detection to point where diagnosis would have been made without screening. Depends on length of pre-clinical phase, frequency of testing, and the test sensitivity
- Length bias: Cases with a disease with a longer natural history are more likely to be detected by a screening programme. But these cases also have a better prognosis. Thus screening leads to a better prognosis, regardless of whether screening itself confers any benefits

- Selection bias: selection, referral or volunteer bias results in a selected subset of the population being screened

Screening Programmes in NZ

- National screening programmes:
 - Neonates: inborn errors of metabolism – Guthrie Card (See Genetic Testing, page 465)
 - Cervical Cancer (See Cervical Cancer, page 351)
 - Vision/hearing testing at school entry (erratic)
 - Mammography (see Breast Screening, page 382)
- Controversial and not currently recommended population screening programmes:
 - Prostate (PSA)
 - Colorectal cancer
 - Otitis media with effusion
- Current screening pilots: Hepatitis B
- Opportunistic screening
 - Antenatal screening
 - Blood pressure
 - Cholesterol
 - Blood glucose
 - HIV
 - Osteoporosis
 - Glaucoma, etc
- Deciding to implement a screening programme:
 - The decision to implement a population based screening programme is complex, must be justified on the basis of standard WHO criteria and supported by research evidence
 - The rules to do with population health are NOT those of an individual clinician (ie just because you would screen an asymptomatic man for prostate cancer is not a reason to implement a national programme)
 - Potential to do harm at a population level is considerable ('first do no harm')
 - We are 'imposing' something – need sound evidence

Ethical Considerations

- Costs and benefits:
 - Costs should include adequate support, counselling, etc. Benefits should include quality of life (but subjective)
 - Many harms are personal – false alarm, false reassurance. Difficult to account for
- Justice:
 - Distribution: benefits accrue to a few and are large; harms fall on many and are minor. Is this fair?
 - Inconvenience borne by many to benefit the few – but this also benefits the group (social welfare function)
 - Collective gains depend on high levels of individual participation
- Autonomy:
 - Motivation: altruism only effective if participants well informed/educated
 - Imposition: Opt-out strategies – trade-off between recruitment level and maximal choice
 - Results: safeguards on third party disclosure
- Opportunistic screening:
 - Cost and benefit usually borne by the same individual
 - Offered responsively rather than proactively
 - Appropriate treatment or other follow-up available
 -
- For Prostate Screening, see Prostate Cancer Screening*, page 225. Prepared for Public Health test.

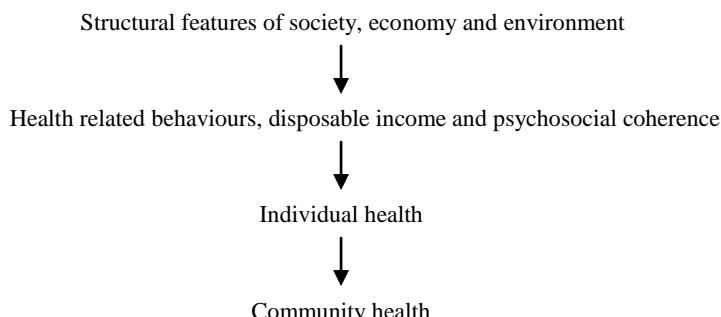
Health Promotion

- = Health promotion is the “process of enabling people to increase control over, and to improve, their health” (Ottawa Charter)
- Ottawa Charter had 5 strategies:
 - Build healthy public policy
 - Create supportive environments

- Strengthen community action
- Develop personal skills
- Reorient health services
- The Treaty Understanding of Hauora in Aotearoa NZ (TUHANZ) is a framework adapting this to NZ (issued by the NZ Health Promotion Forum):
 - Goal for Article 1 (kawanatanga/Governance): achieve meaningful Maori involvement in all aspects of health promotion
 - Goal for Article 2 (Tino rangatiratanga/Maori control and self-determination): actively support the advancement of Maori health aspirations
 - Goal for Article 3 (Oritenga/Equity): Prioritise health promotion action that improves Maori health outcomes
- Progress has been made on: Heart disease, SIDS, Road traffic accidents, cervical cancer
- Issues of concern: Maori to non-Maori gap, melanoma, youth suicide, obesity, ↑STDs
- Compared to other OECD countries, NZ has high mortality from ischaemic heart disease, respiratory diseases, breast and bowel cancers, MVA, suicide
- Role of health care sector:
 - See patients as part of a community, not just as individuals
 - Integrate with programmes delivered by others
 - Move to a focus on the determinants of health (including socio-economic status – income and housing – culture, health care system, in addition to genetics, etc)
- Strategies in the health care sector:
 - Care and support
 - Screening: eg alcohol in pregnancy, cervical, six week check, opportunistic screening for diabetes, breast screening
 - Immunisation: childhood and influenza
 - Health education: eg antenatal education including sun protection, diabetes, HIV, nutrition, exercise, smoking
 - Helping to build healthy public policy
 - Creating healthy institutions (eg Healthy Hospitals – integrating health promotion into their work)
- Barriers:
 - Insufficient time with patients
 - Perceived or real cost disincentives
 - Uncertainty among providers about the evidence

Social Inequalities in Health

- Deprived social and economic conditions strongly associated with poor health
- There is a social gradient in health – it exists in all countries but the slope varies



- Targets for intervention:
 - Socio-economic status: issues around distribution
 - Intermediary factors: housing, targeted support
 - Health issues: access. Most countries target their intervention here
 - Link from Health to SES: disability support
- Poor health → deprivation through stigma and ↓earning potential
- Deprivation → poor health through the following:

Effect of Deprivation on Health

- Poor access to health care:
 - Culturally foreign
 - Financial barriers: GP services, transport, class and language differences between doctor and patient
- Income:
 - Key SES lever. Can have a rapid effect on:
 - Effects of a drop in absolute income
 - Rise in income inequality → divisive effect on society → alienation of ‘work poor households’:
 - Measured by the Gini Co-efficient for household equivalent disposable income
 - Has ↑ for NZ since 1988 from 0.26 to 0.33 (biggest change in the OECD)
 - Is followed with a small lag by indicators such as youth suicide, youth unemployment, etc
 - Formation of social capital. People in ‘survival’ mode don’t have energy to contribute to community
 - Policy levers: monitoring income inequality, change tax rates and social wage, alter WINZ rules about supplements
 - Single parent families, women, Maori and Pacific Islanders are over-represented in the poor
- Education: Increases human capital. Students from poor households are more likely to underachieve, have lower participation rates in tertiary education.
- Occupation and labour force participation:
 - Translates human capital into income. Also indicator of social class
 - Higher injury rates in low SES jobs (forestry, construction)
 - Unemployment: ↑ stress, social isolation, lack of purpose → ↓ self esteem
- Housing:
 - Impacts of rent, neighbourhood, number of bedrooms, quality of construction and maintenance (eg insulation, ventilation).
 - Issue for the poor, and also for former institutionalised psychiatric patients
 - Damp housing → respiratory illness, overcrowding → infectious diseases, ↑ mental distress
- Feelings of hopelessness and being devalued → less cohesive society → violence, exploitation, drug use
- Ethnicity:
 - Interacts with SES
 - Sensitive policy area
- NZDep (NZ Deprivation Index) is a composite measure of deprivation
- Individual health risks:
 - Adequate food in sufficient quantities ('food security')
 - Physical exercise: affected by range or sports facilities, clubs, etc
 - Alcohol/tobacco consumption: affected by taxes, restrictions on distribution
 - Early pregnancy
 - Also indicators such as obesity, high blood pressure, high cholesterol, diet, exercise
- Health behaviours/At-risk behaviour (eg lifestyle factors)
 - Health damaging behaviours more common in low SES
 - Knowledge alone insufficient to change behaviour (eg smoking may be a coping strategy)
- Relate these factors to health status using measures of mortality, morbidity (including measurement of self-rated health status, suffer from specific diseases or measure role limitation), health risks, health service utilisation
- NZ approach:
 - Monitor social and economic determinants of health
 - No systematic cross country comparisons
 - Slow policy development and implementation
 - Lacks cross party and public support
 - Emphasis on health providers not determinants
- Conclusions:
 - Socio-economic determinants of health are multi-causal
 - Issues around policy making under conditions of uncertainty
 - Policies should be monitored against goals

Maori Health

- Includes 2nd and 3rd year PDS notes on Maori Health

Who is Maori*

- 3 concepts:
 - Biological: amount of blood
 - Descent: descended from a Maori but not worried about %age of blood
 - Cultural identification: group to which individual feels most closely aligned
- Ethnic Classification in the Census:
 - Prior to 1974: based on > 50% Maori blood
 - Till 1986: Based on descent
 - 1986 census: What is your ethnic origin (ie self-identification)
 - 1991 census: What ethnic group do you belong to
 - All leads to differences in the way trend data are presented (ie adjustments made to the denominator)
- World-view:
 - Io (supreme being)
 - Te korekore (the nothingness at the beginning)
 - 3 realms which interpenetrate each other:
 - Realm of ultimate reality: Io, Rangi (sky father), Papa-tua-nuke (earth mother), Tipuna (Gods, spirits, ancestors), mana and tapu
 - Realm of the human
 - Realm of the dead
- Mana:
 - Enduring, indestructible power of the Gods
 - Mana atua: sacred power of the Gods
 - Mana tupuna: power or authority handed down through chiefly lineage
 - Mana whenua: power associated with possession of lands
 - Mana tangata: power acquired through developing skills
- Tapu:
 - Sacred, set apart, forbidden, restricted
 - Everything created by gods has Tapu (people, land, river, forests)
 - People become tapu by their desire to stay under the influence and protective powers of the gods
 - There is good tapu and bad tapu (the devil has tapu too!)
 - Compares with noa (free from tapu, common)

Epidemiology

- Life expectancy has improved compared to Pakeha since 1950, has levelled off, and is now about 10 years less than Pakeha
- Maori have worse health statistics but fewer hospitalisations (ie use services less)
- Wide disparities across all indicators of Education, health, income, housing, employment and criminal justices
- Maori concentrated in lowest 3 deciles of deprivation index – 25% in lowest
- When controlling for deprivation, Maori life expectancy is still worse, and gets even worse in the lowest decile ⇒ Maori are not just sick because they're poor. Possible explanations:
 - Not Maori behaviour – common to ethnic minorities around the world
 - Not genetic – why would Maori and black Americans have the same predispositions given the degree of genetic separation
- Social and economic determinants of health:
 - Michael Marmot: epidemiology of British civil service – position in hierarchy better predictor of life expectancy than smoking, hypertension, etc
 - Postulate: Don't have more problems but have fewer choices → chronic stress from poor control over life (can only worry, can't do anything else) → elevated hormone response (eg Corticosteroids) → lipids, obesity, insulin resistance, CHD, etc. Effectively aging quicker.
 - Stress levels impact on the degree of impact of lifestyle factors on your health
- Urban shift:
 - In 1945, 25% of Maori lived in urban areas. In 1980, 80% lived in urban areas

- Due to development of manufacturing industries and centralisation of agricultural production (eg freezing works) → fewer jobs in traditional tribal areas

Reasons for smoking

- Part of history: tobacco given as gifts at Waitangi, Goldie images of smokers, etc
- Advertising: eg Howard Morrison (role model) advertising lighters
- It has become culturalised: carved pipes, woven pouches for lighters → reinforce link between smoking and Maori
- Responses:
 - Smoke free hui
 - Aim at young ('Why start') – counter image that its cool to smoke
 - Smoke free areas
 - Enforce bans on underage sales
 - Needs whanau, local, national integration

The Treaty of Waitangi (Te Tiriti O Waitangi)

- Pre-treaty history:
 - Increasing availability of guns and overcrowding in the north → ↑inter-tribal wars
 - Introduced diseases → high mortality
 - 1831: Chiefs wrote to the king to ask for protection. Busby sent as NZ resident in 1832
 - 1835: Northern tribes declaration of independence
 - 1839: Hobson sent by colonial office to do a new deal
- At the time of the treaty:
 - Maori significantly outnumbered non-Maori
 - Settlers wanted land
 - Maori needed British government to control sailors, whalers and convicts who came here
 - Maori needed national identity to trade inter-nationally (eg ships needed a flag)
 - Maori and non-Maori had a mutual need for each other
- The Treaty:
 - 1. Kawanatanga (Governance) vs Sovereignty in English – no Maori would have given this up
 - 2. Tino Rangatiratanga (Chieftainship, Control, Autonomy) vs Possession in English
 - 2a: Queen promised protection, and exercise of their chieftainship over lands, villages and treasures
 - 2b: Queen had exclusive right to buy land (and sell it on at a profit to finance the colony)
 - 3. Oritenga: Equity
- Application of Treaty to health:
 - Implicit in treaty were concepts of equity, partnership, economic and cultural security
 - Concepts of health firmly based in Maori culture, which under the treaty are recognised and protected
 - Kawanatanga (Governance): Government has responsibilities to govern and should take reasonable steps to improve health. Crown has obligations as well as power. Applies to all citizens
 - Tino Rangatiratanga (Chieftainship, Control, Autonomy). Applies to Maori. Right to establish and provide services (but its not just a right, it is also effective)
 - Oritenga: Equity. Maori have poorer health and poorer access, so neither equality of opportunity nor outcome
- Post Treaty:
 - Treaty was basically sound – but the Crown didn't stick to it:
 - Others brought land directly
 - Crown brought land unfairly or confiscated it
 - Maori discriminated against in social policy, entitlement to vote, treatment of returned servicemen, etc
 - 1841: unused land deemed Crown land
 - 1844: law enabling Maori to be educated in English. Speaking Maori in school punishable offence till relatively recently
 - 1852: right to vote given to individual land owners – Maori excluded as land held collectively
 - 1863: law allowing confiscation of the land of rebels
 - 1867: ↑Maori individual ownership of land → threat of majority in some electorates → set up 4 Maori sets so Maori remain a minority

- Rapid loss of land (from 26.8 m hectares to 3 m hectares by 1900), ↑Pakeha, concern among Maori about loss of clout → Kingitanga movement
- Land wars in Taranaki and Waikato: complex and changing politics, many tribes at one point or another were allied with the British against Maori enemy tribes

Impact on Health

- Socio-economic: low incomes, poorer housing, higher unemployment, less education
- Lifestyle: diet smoking, alcohol, drug use
- Cultural factors: alienation, loss of wairua and cultural identity, urban drift → fragmentation of whanau
- Due to:
 - Failure to give same rights and privileges
 - Failure to protect treasures
- See also Maori Mental Health, page 410

Cornerstones of Maori Health

Cornerstones

- Attempt to get away from purely bio-medical model of health
- Taha hinengaro: mind and emotions
 - Includes cultural identity: Te whanau (family), te whenua (land) and te reo (language)
 - Mana important to maintenance of mental health
 - Whakama: encompasses shyness, embarrassment, shame. Confused with depression, guilt, subordination
- Taha wairua: spiritual health
 - Life force: reflects where you come from, guides your future
- Taha tinana: physical health
 - Tapu: complex: places/objects (eg tiki)/body parts (head & genitals)
 - Don't mix food and heads, 2 ends of GI tract should never meet
- Taha whanau: family.
 - Belonging, identity, security
 - Whakapapa: whanau → hapu → iwi
 - Fragmented by urbanisation
 - Check family and social history (eg family effected by mental illness, family health impacts on personal health eg abuse, etc)
- Eg – application to type 2 diabetes:
 - Taha hinengaro: Need understanding to manage disease and prevent disability, needs coping strategies
 - Taha wairua: colonisation and cultural dislocation → cultural identity and recovery: need a passion to live, to know their place in the world → more likely to beat the illness
 - Taha tinana: Medical response, treatment of complications
 - Taha whanau: Family breakdown contributes to poor lifestyle and support. Need support of family in making lifestyle changes

*Other factors **

- Tino rangatiratanga: control of own destiny
- Economic security
- Self esteem, pride and confidence
- Measures of Maori health: value of resources in Maori ownership, drop in crime rate, use of te reo
- Tohunga: traditional Maori healer (common in Maori communities)
- Mate Maori: illness due to wrong doing → refer to kaumatau

Death and Dying *

- For family and friends, seeing the patient while alive is important, bring koha, say karakia
- Following death:
 - Everything is tapu – those at the bedside are responsible for ensuring customs carried out
 - Avoid post-mortem: sanctity involved, impedes release of spirit (spirit lingers 3 – 8 days)
 - Dead person never left unattended
- Tangi:
 - 2 – 5 days after death

- Farewell speeches and lamenting
- Conflict over where to bury the deceased: te tupapaku may be taken to a number of marae as a compromise
- Encourage wairua to depart
- After burial: hakari – sacred feast – turning point

Maori services

- Tipu Ora: in Rotorua, building on traditional role of ‘Kuia’ (“nanny”) – Maori, non-smoking, young grandmothers. Pragmatic focus (ie get them to smoke outside rather than insisting on smoking cessation). Has reduced SIDS

Maori Cultural Differences

- Contributing factors to cultural dislocation:
 - Perceived value of self
 - Social position
 - Cultural dislocation → shattered spirituality → ↓Taha wairua
 - Ignore cultural values and they'll ignore you
- Responses:
 - Don't blame – beating up on beaten up people doesn't change anything
 - Give them resources: e.g. to population group (cf. AIDS control)
 - Use cornerstones on consultation check list
 - Are we contributing to peoples stress or reducing it?

Drug and alcohol policy

- See also Regulation of Medicines and Drugs, page 535
- See also Cannabis/Marijuana, page 448
- Drug epidemiology:
 - Deaths attributed to drug use:
 - 79% Tobacco
 - 19% Alcohol
 - 1 % Other drugs
 - Male deaths twice female deaths
 - Social costs (including lost production, mortality, health costs, benefits from consumption etc) reveal alcohol is more ‘expensive’ than tobacco (Tangible and intangible costs of alcohol = 6% of GDP, tobacco = 4.9%). Alcohol takes people from production and has greater secondary costs (on family, accidents, etc, and effects production from earlier in life)
- Prevention Paradox: To get greatest gain from prevention need to target the mean, not the tail (although they drink the most), as most people, and therefore the biggest cost, relates to people around the mean. (Eg cholesterol, alcohol, etc)
- Historical influences:
 - Colonial society: more men than women (miners, whalers, etc)
 - Brewing industry and pubs a large employer of labour
 - Brewing industry characterised by wealthy and influential families
 - Other communities had other drugs (Chinese – opium, Italians – wine, which were subject to different regulations)
 - ↑Women settlers in later 19th century → saw alcohol as a problem → strong temperance movement → push for ↑ regulation in early 20th century
- Interests/stakeholders in drug policy today:
 - Politicians: libertarian vs conservative
 - Legal drug companies: tobacco/alcohol (invest \$\$ into ‘education’ to control the climate of what is ‘cool’)
 - Illicit drug dealers: large gang involvement
 - School sector: teachers/principals
 - Medical profession (also issues around medicinal use, eg of cannabis)
 - Lobby groups: ASH, DARE, Drug foundation, Life Education Trust
 - Police: \$30 mill per year for cannabis control, 12,000 arrests for cannabis offences, 6000 prosecutions, only 500 get diversion
 - Maori: 2 views: its dangerous so should be illegal vs it is criminalizing young Maori

- Cannabis: have had a debate without good information

Health Economics

- = The study of how individuals and societies, experiencing virtually limitless wants, choose to allocate scarce resources to best satisfy their wants
- Scarcity:
 - Resources (main factors of production – natural resources, capital, labour) are scarce
 - → Goods and services produced from them are scarce
 - Can't have as much as we would want if they are free
 - Will always be medical interventions that cannot be funded
- Choice: Because of scarcity, we must make choices
- Opportunity cost:
 - The loss of the next best opportunity we could have chosen (ie if we use time/money on one thing, it's not available for something else)
 - When doing an evaluation: deduct GST (it's a transfer), use real price (eg not subsidised cost of a drug), include indirect costs (eg patient travel)
 - Can be calculated from different perspectives: eg provider, funder, society
- Marginal analysis:
 - = Incremental benefit (ie marginal benefit) from incremental cost (ie marginal cost)
 - Decisions are usually about whether to expand or contract – not stop or start
 - Marginal cost is NOT the same as average cost
- Efficiency:
 - = Maximising benefits from certain cost of inputs
 - Not the same as cost-cutting: if you cut costs and output falls then haven't improved efficiency
 - Effectiveness: are patients better off (eg have better health) with intervention than without
 - Technical efficiency: providing effective services at least cost – doing things right
 - Allocative efficiency: concentrating resources on effective services that offer the biggest payoff in terms of health – doing the right things
 - Inefficiency is unethical (if budget is constrained)
- Equity:
 - = Fairness: usually of distribution or payment
 - Equal access for equal need (what is need – ill health or capacity to benefit)
 - Equal resources for equal need (same amount of money for equal needs – basis of the DHB funding formula)
 - Equal outcomes: allocate resources to achieve same health status of different populations
- Markets:
 - Means of allocating scarce resources
 - Result from the interaction of demand and supply, mediated by price
 - Consumers can signal demands, maximise their 'well-being' or utility, producers can shift resources accordingly
 - If there is perfect competition, theoretically you get allocative efficiency
 - For this to work, requires:
 - Perfect information (eg about quality, costs, etc)
 - No externalities (someone else bears a cost or benefit)
 - Goods and services must be rival in consumption (ie if I buy it no one else can have it) and excludable (you can't have it if you can't pay)
 - Freedom of entry and exit
 - Perfect competition – no monopolies
 - No supplier-induced demand
 - Equity is not an issue (ie no merit goods – goods that society believes should be more widely available than would occur through markets alone)
 - Market failure in health care:
 - Externalities eg immunisation
 - Monopolies eg secondary services, labour markets
 - Asymmetric information eg health professionals
 - Supplier induced demand (especially if fee-for-service)
 - Highly inelastic demand
 - Health Insurance Markets

- Uncertainty about future health needs + high costs → demand for insurance
- Moral Hazard: will now consume more health care than they otherwise would as someone else is paying (can control with co-payments)
- Adverse selection: patients who know they will need it are more likely to purchase it. Insurers won't know so premiums won't reflect risk
- Want to get advantages of market efficiency and overcoming market failure → ?government failure, purchaser provider splits, quasi markets (health care plans)
- International Comparisons: Health Expenditure per capita and GDP. NZ is on the line
- Economic Evaluations :
 - = Comparative analysis of alternative courses of action in terms of their costs and consequences
 - Informs choices about the allocation of scarce resources
 - Needed to determine efficacy (in lab conditions), effectiveness (more good than harm in practice)
 - Can be prospective or retrospective
 - Types of evaluation:
 - Cost minimisation: compare inputs, assume outputs are equal
 - Cost benefit: compares different outcomes (eg flu jabs and hypertension screening). Convert to common unit (\$) to compare – but can human life be valued?
 - Cost effectiveness: relates cost to a clinical measure (eg ↓blood pressure, morbidity, life years gained). Has superseded cost-benefit analysis due to problems allocating monetary values to all outputs
 - Cost utility: cost per QALY gained. Can compared across a whole range of interventions – but methodological problems. Example: Impact on QALYs of dialysis versus kidney transplant.
- Common approaches to valuing human life:
 - Human capital: future earnings (but elderly have none)
 - Implied valuations: value implicit in past policies
 - Insurance values: but this is paid to survivors
 - Willingness to pay to reduce low probability of death: survey or observe (eg how much do people spend on safety)
- Theory X and Y: Summarising different approaches to health care in health economics

	Theory X	Theory Y
View of Health	Health and disease occur randomly	Health determined by lifestyle choices
Medical Care	Special. Market Failure	Same as other goods and services
Practice of Medicine	A Science	An art
Economics	Financial rewards reduce the quality of caring	Financial rewards generate high quality care
Policy	Regulation needed to mitigate economic forces. Tax the healthy, subsidise the sick. Discourage new medical technologies	Reduce regulation, encourage market forces. Tax the sick, not the healthy. Encourage new technologies

Evidence Based Medicine

- Reference: 4th Year Evidence Based Medicine Notes

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Introduction

What is Evidence Based Medicine

- = ‘The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. This practice means integrating individual clinical experience with the best available external clinical evidence from systematic research’
- Why is it necessary:
 - Wide variation in clinical practice
 - To minimise clinical error
 - High use of treatments not proven to do more good than harm
- Can be extended from medicine to health care
- Need to understand new types of evidence: randomised controlled trials (started in 1948), meta-analysis and systematic reviews
- EBM approach is better than traditional continuing medical education (which is largely ineffective). Clinical knowledge and performance deteriorates over time
- Application of evidence:
 - Generalisability: do trials apply to a whole population
 - Applying probabilities from a population to an individual
 - Multiple treatments: trials only test one at a time
 - Acceptability
 - Also need to consider economic impact given limited resources

Developing a CAT (Critically Appraised Topic)

- Title: Answer to the clinical question that initiated the search
- Clinical Scenario: brief summary of the context in which the question arose
- The clinical bottom line: a description of the clinical action to be taken as a result of the critical appraisal
- Well Built Question: good for defining pre-test probability and narrowing search strategy
 - The Patient or problem being addressed in what setting (e.g. In otherwise healthy, non-smoking adults presenting to a GP with a common cold...)
 - The intervention being considered (...does a 5 day course of XX)
 - The comparison intervention (where relevant) (...compared with a placebo...)
 - The clinical outcome of interest (...improve symptomatic control and/or reduce the duration of an existing common cold)
- Search The Evidence: list search terms
- Description of study methodology
- Table summarising key results
- Quantitative take home messages
- Notes on validity issues: bias, levels of evidence, research design and methodology, harmful effects of intervention, etc
- References to the articles used in the critical appraisal

Cochrane Collaboration

- Aims:
 - Evidence based
 - Easily accessed
 - Clinically useful
 - Quality controlled
 - Periodically updates
- Prepares, maintains and disseminates systematic reviews.
- Systematic reviews are a structured process:
 - Well formed question
 - Comprehensive data search (including non-English, unpublished)
 - Unbiased selection and abstraction process
 - Critical appraisal of data
 - Synthesis of data
 - Width of diamond on Cochrane logo = confidence interval of meta-analysis

Levels of Evidence

- 1 – RCT or reviews of them
- 2 – Cohort studies or reviews of them
- 3 – Case control studies
- 4 – Case series or poor quality cohort or case-control studies
- 5 – Expert Opinion

EBM Glossary

- Bias: systematic deviation of study results from true results due to the study design.
 - Interviewer bias: systematic error due to interviewer's gathering of selective data.
 - Lead time bias: if patients not enrolled at similar point in their illness, differences in outcome may only reflect differences in duration of illness.
 - Recall bias: systematic error due to differences in accuracy or completeness of recall. Referral filter bias – process of referral from primary to secondary ↑ proportion of severe cases → ↑unfavourable outcomes.
 - Selection bias: a bias in study design rather than chance when study and control groups differ in ways that may affect the outcome
 - Publication Bias: results from studies with positive results are more likely to be published
- Study types:
 - Case-Control Study: retrospective comparison of exposures of persons with disease and without disease
 - Prospective Study: cohorts who have not yet had the outcome event are monitored for the occurrence of the event
 - Systematic Review: study in which trials on a topic have been systematically identified, appraised and summarised according to predetermined criteria. May or may not include a meta-analysis combining the results of the trials
- Clinical Practice Guideline: systematically developed statement to assist decision-making in specific clinical circumstances
- Study Design:
 - Decision Analysis: application of explicit, quantitative methods to analyse decisions under conditions of uncertainty
 - Intention to treat analysis: analyses individuals according to the group to which they were randomised, even if they didn't receive the treatment, rather than confining to those who completed treatment (treatment may have intolerable side-effects). Better measure of effectiveness.
 - N-of-1 trials: blinded patient and doctor undergoes pairs of treatment periods with experimental and placebo treatment with outcomes monitored
- Study Analysis:
 - Confounding: a variable associated with the factor under investigation. Unless it is possible to adjust for the confounding variables, their effects cannot be distinguished from those of the factors being studied
 - Efficacy: benefit of an intervention under ideal conditions
 - Efficiency: benefit of intervention, including efficacy and acceptance (e.g. compliance, side effects – does it do more harm than good)
 - Precision: the range in which the best estimates of a true value approximate the true value
 - Statistical power: statistical chance of a study being able to detect a difference if one actually exists
 - Strength of inference: likelihood that an observed difference represents a real difference, rather than due to chance. Is weakened by bias and small sample sizes
 - Validity: results are unbiased and give true estimate of the measured effect. Extent to which a variable or intervention measures or accomplishes what it is supposed to. Does it measure what it claims to measure – described by specificity and sensitivity, etc

Risks and Odds

Exposure	Outcome	
	Yes	No
Yes	A	B
No	C	D

- Event Rate: proportion of patients in a group in whom an event is observed. Applied to Controls and Experimental groups → CER and EER
- Relative Risk = $(A/(A+B))/(C/(C+D)) = EER/CER$
- Absolute Risk Reduction (ARR) = $C/(C+D) - A/(A+B) = CER - EER$
- Relative Risk Reduction: percent reduction in events in the treat group event rate compared to the control group = $(CER - EER)/CER * 100 = (C/(C+D) - A/(A+B))/(C/(C+D))$
- Risk Ratio = EER/CER Odds: ratio of events to non-events
- Odds ratio: odds of an experimental patient suffering an adverse event relative to a control patient = $(A/C)/(B/D)$
- Number needed to treat (NNT): number of patients needing treatment to achieve one favourable outcome = $1 / ARR$ – always rounded up to the nearest whole number and accompanied by the 95% CI
- Number needed to harm (NNH): number of patients who need to be treated to achieve one adverse outcome = $1 / \text{Absolute Risk Increase (ARI)} = EER - CER$
- RRR and OR do not say anything about absolute risk. An RR of 30% can mean a risk reduction from 60% to 20%, or from 3% to 1%. The ARR and NNT varies dramatically
- Time frame: all measures (RR, RRR, ARR, OR) must be qualified by giving them a time frame (e.g. the length of the period of the study)

Evaluation of History Taking and Clinical Examination

Using an article about history taking or clinical examination

- See Using an article about a diagnostic test, page 706

Kappa Statistics

- A measure of agreement after chance is removed from consideration
- = Actual agreement beyond chance / potential agreement beyond chance:
- E.g.. If observed agreement = 78% of cases, and agreement on the basis of chance is 51%, then Kappa = $(78 - 51)/(100 - 51) = 0.55$

Kappa Statistic	Degree of Agreement
-1	Perfect disagreement
0	Chance agreement
0 – 0.4	Poor agreement
0.4 – 0.6	Moderate
0.6 – 0.8	Substantial
0.8 – 1.0	Almost perfect

- Hard to compare between studies – a different case-mix would yield a different k
- A weighted k can be used to measure agreement in ordinal data
- For larger samples (> 100) sampling distribution is normal, so it is possible to calculate a standard error, confidence intervals and P values
- Other non-parametric tests (e.g. chi-squared, correlation coefficient) are measures of association not agreement

Evaluation of Diagnostic Tests

Sensitivity and Specificity

- Sensitivity: proportion of people with disease who have a positive test (i.e. true positive). How good is the test at picking up people who have the condition? SnNout = when a test has a high sensitivity, a negative result rules out the diagnosis
- Specificity: the proportion of people free of a disease who have a negative test (i.e. false positive). How good is this test at correctly excluding people without the condition? SpPin = When a test is highly specific, a positive test rules in the diagnosis
- Necessary Sensitivity and Specificity depend on setting. E.g. if screening for a disease occurring 1 in 10,000 in a population of 100,000 then a test with sensitivity of 99% and specificity of 99% will find 9.9 true positives and 999.9 false positives. But if the disease occurs 1 in 100 then you'll find 9990 true positives and 998 false positives – far better strike rate

Pre-test Probability

- = $P(D+)$ = probability of target disorder before a diagnostic test result is known. Depends on patient (history and risk factors), setting (e.g. GP, A&E, etc) and signs/symptoms
- Is useful for:
 - Deciding whether to test at all (testing threshold)
 - Selecting diagnostic tests
 - Interpreting tests
 - Choosing whether to start treatment without further tests (treatment threshold) or while awaiting further tests
- Based on epidemiology (e.g. prevalence) or clinical experience

Likelihood Ratio

- Positive Likelihood Ratio = the likelihood that a positive test result would be expected in a patient with the target disorder compared to the likelihood that the same result would be expected in a patient without the target disorder
- Negative Likelihood Ratio = same but for negative result
- Less likely than sensitivity and specificity to change with the prevalence of a disorder
- Can be calculated for several levels of the symptom or test
- Can be used to calculate post-test odds if pre-test odds and LR known
- Impact of LR:
 - < 0.1 or > 10: large changes in disease likelihood (i.e. large change to pre-test probability)
 - 0.2 – 0.5 or 2 – 5: small changes in disease likelihood
 - 1: no change at all

Post-test Probability

- = Proportion of patients with a positive test result who have the target disorder
- Positive Predictive Value (+PV): proportion of people with a positive test who have disease. If the person tests positive, what is the probability that s/he has the disease? Determined by sensitivity and specificity, AND by the prevalence of the condition
- Predictive value of test depends on sensitivity and specificity AND on prevalence. E.g., for a test with 99% sensitivity:

Prevalence	Positive Predictive Value
1	19
2	33
5	56
10	73
20	86

- So significance of test may vary between, say, hospital and GP

Formulas

	Diseased	Normal
Test +ive	a	b
-ive	c	d

$$\text{Sensitivity} = a/(a+c)$$

$$\text{Specificity} = d/(b+d)$$

$$\text{LR}^+ = \text{sensitivity}/(1-\text{specificity})$$

$$\text{LR}^- = (1-\text{sensitivity})/\text{specificity}$$

$$\text{Positive Predictive Value} = a/(a+b)$$

$$\text{Negative Predictive Value} = d/(c+d)$$

$$\text{Prevalence} = (a+c)/(a+b+c+d)$$

$$\text{Pre-test odds} = \text{prevalence}/(1-\text{prevalence})$$

$$\text{Post-test odds} = \text{pre-test odds} * \text{LR}$$

$$\text{Post-test probability} = \text{post-test odds}/(\text{post-test odds}+1)$$

$$\text{Accuracy} = (a+d)/(a+b+c+d) = \text{what proportion of results have given the correct result}$$

Study design for researching a test

- Spectrum composition: what population was it tested on. Sensitivity and specificity may vary between populations with significant disease and the general population
- Are pertinent subgroups assessed separately? Condition for test use must be narrowly defined to avoid heterogeneity
- Avoidance of work-up bias: if there is bias in who is referred for the gold standard. All subjects given a test should receive either the gold standard test or be verified by follow-up
- Avoidance of Review Bias: is there objectivity in interpretation of results (e.g. blinding)
- Precision: are confidence intervals quoted?
- Should report all positive, negative and indeterminate results and say whether indeterminate ones were included in accuracy calculations
- Test reproducibility: is this tested in tests requiring interpretation

Using an article about a diagnostic test

- Is the evidence about the accuracy of a diagnostic test valid?
 - Was there an independent, blind comparison with a reference standard?
 - Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice
 - Did the results of the test being evaluated influence the decision to perform the reference standard?
 - Were the methods for performing the test described in sufficient detail to permit replication?
- Does the evidence show the test can accurately distinguish between those who do and don't have the disorder? Are the likelihood ratios for the test results presented or data necessary for their calculation provided?
- Can I apply this test to a specific patient?
 - Will the reproducibility of the test and its interpretation be available, affordable, accurate and precise in my setting? Is interpretation of the test tested on people with my skill level?
 - Can I generate a sensible estimate of the patient's pre-test probability?
 - Are the results applicable to my patient? (e.g. do they have the same disease severity)
 - Will the results change my management?
 - Will the patients be better off as a result of the test? An accurate test is very valuable if the target disorder is dangerous if undiagnosed, has acceptable risks and effective treatment exists

Bayesian Theory

- Combining information from history, exam and investigations to determine overall likelihood
- Puts test results in context
- Use as part of decision analysis to determine the level at which the probability of disease is sufficiently low to withhold treatment or further tests, or sufficiently high to start treatment. In between, do further tests to raise or lower probability
- Balance between: severity of illness, efficiency, complications of test and treatment, and properties of the test

Evaluation of Therapy

Assessment of an article about Therapy

- Are the results of the study valid?
 - Was the assignment of patients to treatments randomised?
 - Was follow-up complete? (Non-follow-ups may have died, etc → bias)
 - Were patients analysed in the groups to which they were randomised?
 - Were patients and researchers 'blind' to the treatment
 - Were the groups similar at the start of the trial
 - Other than the intervention, were the groups treated equally?
- What were the results?
 - How large was the treatment effect? RR, RRR, ARR
 - How precise was the estimate of the treatment effect? Point estimate & Confidence intervals.
What is the P value?
- Will the results help me in caring for my patients?
 - Can the results be applied to my patient care?

- Were all clinically important outcomes considered: were the outcomes relevant for the patient? Or was only a benefit to intermediate outcomes considered?
- Do treatment benefits out-weight harms and costs? ARR and NNT/NNH

Evaluation of Prognosis

Glossary

- Prognosis: the possible outcomes of a disease or condition and the likelihood that each one will occur. How to estimate your patient's likely clinical course over time, or anticipate likely complications of the disorder
- Prognostic factor: characteristics associated strongly enough with a condition's outcome to predict accurately the development of these outcomes. E.g. demographic (e.g. age), disease specific (e.g. tumour stage), or co-morbidity (e.g. other conditions present)
- Prognostic results are the number of events occurring over time, expressed in absolute terms (e.g. 5 year survival rate), relative terms, or survival curves
- Risk factor: patient characteristics associated with an increased probability of developing a disease in the first place. Neither prognostic or risk factors imply a cause and effect relationship

Using an article about prognosis

- Are the results of the study valid?
 - Was there a representative and well-defined sample of patients at a similar point in the course of the disease? (ideally at its onset). Is the disease clearly defined (what are the inclusion/exclusion criteria)? Is the sample representative of the whole spectrum of disease? Sources of bias: e.g. selection bias (referrer bias) or lead-time bias
 - Was follow-up sufficiently long and complete (what were the potential characteristics of those lost to follow-up?)
 - Were objective and unbiased outcome criteria used? Were the investigators blind?
 - Was there adjustment for important prognostic factors? Were subgroups with different prognoses stratified?
- What are the results?
 - How large is the likelihood of the outcome event(s) in a specified period of time
 - How precise are the estimates of likelihood? Precision best expressed in confidence intervals
- Will the results help me in caring for my patients?
 - Were study patients similar to my own?
 - Will the results lead directly to selecting or avoiding therapy?
 - Are the results useful for reassuring or counselling patients?

Professional Development

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Professional Boundaries

- Defines proper/improper behaviour in a professional relationship
- Types of boundaries:
 - Physical
 - Emotional: strengthened by right to say yes/no, respect, weakened by ridicule, belittling, judgementalism
 - Sexual: serve to protect most sensitive part of us
- Differences from personal boundaries: Paid for, time limited, power more imbalanced, greater responsibility for maintaining relationship, requires knowledge and training
- Sources of power:
 - Personal power: size, gender, age, strength, skills, intellect, charisma, money, weapons
 - Position power: role, job, money, legal status

Recognising and Respecting Differences

- Sometimes differences obvious, sometimes subtle
- Can lead to misunderstanding, poor compliance
- Avoiding recognition of differences is a way of preventing challenge to our world view

Working in Teams

- 7 components of teams that need to be functioning for the team to work:
 - Raison d'etre: clear idea of what the team is therefore
 - Rules: each person needs to know them
 - Roles: same person often adopts the same role in different teams
 - Relationships
 - Rituals: joining and farewell rituals, birthdays, etc
 - Rewards
 - Results: do you achieve your raison d'etre
- Developmental cycle:
 - Forming:
 - Becoming acquainted: polite, impersonal, hierarchical
 - Trial and error: pairing, turf guarding, role conflict, ambiguity (still working as individuals)
 - Storming:
 - Collective indecision: covert anger, decision by default, poor morale, no accountability/leadership
 - Crisis: open anger, recognition of conflict, leadership assumed
 - Maintenance: commitment to team work
 - Performing: management of conflict, sharing information, tolerance or ambiguity/difference, flexibility, breaking down of inter-professional rivalries
- Power in groups:
 - Always ask 'who holds the power'
 - Positional (assigned from outside the group), assigned, knowledge, personal, factional
- Group processes:
 - Problem solving
 - Decision making: who, when, how, what
 - Conflict management:
 - Competing: It's win/lose and I'm going to win
 - Accommodating: I don't mind losing
 - Avoiding
 - Compromising
 - Collaborating

Physical Hazards of Medicine

- Hospital hazards:
 - Biological (infection control):
 - Blood and body fluid exposure (e.g. risk of seroconversion following needle stick HBV 30%, HCV 3%, HIV 0.3%)
 - Tb (high prevalence → high index of suspicion, wear face mask in high risk situations, ensure contact tracing)

- Meningitis (spread via respiratory secretions, need close contact, wear mask)
- MRSA (spread via direct contact, could be almost totally managed by hand-washing). Manage via vaccination, possible prophylaxis
- First aid after exposure (needle stick, splash, spill, bite): rinse affected area under running warm water for at least 3 minutes, squeeze a puncture wound gently, paint with povidone-iodine or isopropyl alcohol
- Chemical (drugs, latex, hand washing → hand dermatitis: usually irritant dermatitis not allergic dermatitis → dose dependent)
- Ergonomics (patient handling, keyboards)
- Physical (lasers, radiation, heat, noise)
- Stressors (shift work, overload – usually insidious)
- Behaviour:
 - Knowledge doesn't change behaviour
 - Consider own and patient safety
 - Hazard vs. risk vs. perceived risk

Medical Crises

- Need to:
 - Understand and manage our reactions to critical medical incidents
 - Learn methods of debriefing
 - Maintain confidentiality when managing reactions to unusual events
- A crisis can be:
 - Death of a patient: especially if similar age or if relationship has developed
 - Patient complaints, medico-legal action
 - Blaming yourself for bad outcomes
- Responses can be depression, anger, physical illness, ↑use of alcohol or self medicated drugs, isolation, suicide
- Coping strategies:
 - Accept that it is normal to be stressed by stressful events
 - Develop an active interest in details of the crisis (eg read up)
 - Be open about your feelings, don't say you're fine
 - Actively pursue social support, leisure pursuits
 - If medico-legal action, keep close contact with your lawyer and as much contact with the patient as the patient desires
 - Watch out for avoidance behaviours (dropping out, sick days) or intrusive re-experiencing (eg nightmares) –usually indicates need for help
 - Talk to counsellor, GP, colleagues, mentor – not to family or non-medical friends

The Doctor's Health

- Stress = Marked discrepancy between perceived demands and perceived ability to respond
- Burnout = set of symptoms leading to a debilitating psychological condition usually associated with:
 - Chronic stress
 - Emotional exhaustion
 - Depersonalisation
 - Reduced personal accomplishment
 - Development of negative and callous attitudes about the people one works with
 - Negative self worth
 - Result of a prolonged period of trying to cope with demanding stressors
- Medical Practitioners Act: Must notify the Medical Council if you consider a colleague's health is affecting his or her competence
- Doctor is unfit to practice if: unable to make safe judgements, demonstrate reasonable skill, behaves inappropriately, risks infecting patients, etc
- Medicine has many stresses: business demands, patient expectations, difficult patients, mistakes, rosters → tiredness, litigation, ↓time for family
- On population estimates, there should be 200 – 300 medical practitioners who are alcoholic – only about 50 are being treated
- There are many barriers to seeking help: admitting to illness, financial consequences, not wanting to be seen as inadequate, isolation

- Prevention is key: good health habits (especially in hard times), avoid self-treatment – have your own GP, formal and informal peer support, develop interests outside medicine, seek help early
- Resources to help:
 - Doctor's Health Advisory Service (DHAS): partly funded by the medical council
 - In Sickness and In Health: a handbook for medical practitioners

Code of Health and Disability Services Consumer's Rights

- Right 1: Right to be treated with respect (incl. privacy respected and right to services that respect their needs/culture/religion)
- Right 2: Right to freedom from discrimination, coercion, harassment and exploitation
- Right 3: Right to dignity and independence
- Right 4: Right to services of an appropriate standard (incl. co-operation among providers)
- Right 5: Right to effective communication (incl. right environment and interpreter if necessary)
- Right 6: Right to be fully informed
- Right 7: Right to make an informed choice and give informed consent
- Right 8: Right to support (ie to have support people present if at all possible)
- Right 9: Rights in respect of teaching or research – all other rights extend to when patient is participating in research or teaching
- Right 10: Right to complain
- Provider compliance:
 - A provider is not in breach of this code if they have taken reasonable actions in the circumstances to comply with duties in the code
 - The onus is on the provider to prove that it took reasonable actions
 - Relevant circumstances includes consumer's clinical situation and the provider's resource constraints

Medical Error and Misadventure

- Medical mishap = treatment was properly given but suffered a rare side-effect (<1% occurrence) and was severe (ACC definition is in hospital for at least 14 days, in incapacitated for 28 or died)
- Medical error = Person treating you did not provide treatment of a reasonable standard.
- Medical misadventure = mishap + error
- Negligence:
 - Do you owe a duty of care
 - Did you fail in that duty (according to standard of a reasonable practitioner)
 - In failing, did the person suffer as a consequence
 - Court decides whether error is negligence
- Types of censure:
 - From Health and Disability Commissioner (mediate, refer to professional body, referral to their director of proceedings)
 - From Medical Council (censure, practice restrictions, struck off, fines)
 - Criminal charges – eg Manslaughter – only if 'major departure' from accepted practice (1997 Crimes Act amendment)

Medical Council

- Protects public by determining competence of and registering doctors
- To be registered must have: acceptable degree, competent in English, no convictions with a possible prison term > 3 months, be mentally and physically fit and not subject to disciplinary proceedings
- Types of registration include: probationary, general, vocational
- Council can review or monitor competence or 'fitness to practice'
- Also has disciplinary process
- Council consists of 4 doctors elected by doctors, 4 people appointed by the Minister, 1 Ministry of Health and 1 Med School Dean.

Certification of Death

- Confirm identity of patient
- Signs of death:
 - No circulation: no carotid pulse or heart sounds over 1 – 3 minutes
 - Absent respiration: no movement or fogging of a mirror
 - Unreactive pupils

- ‘Railroading’ of retinal blood vessels – rows of RBCs settling out
- Absence of pattern on EEC or ECG
- Signs of brain death (ie on respirator)
 - Fixed dilated pupils
 - No corneal reflex
 - No tracheal reflex (ie tug on ET tube)
 - No eye movements on putting cold water in ear
 - No Cranial nerve response to pain (eg supra-orbital pressure)
 - No respiratory response to hypercapnea
- Problems when deeply unconscious: near drowning, hypothermia, epilepsy, drugs (eg barbiturate poisoning)
- Suspicious injuries on a dead person: bruise, abrasion, laceration, incised wounds (suicide look for tentative cuts, assault look for defence injuries), stab wounds (go deeper than the length of the blade, always check), pattern wounds
- Person certifying death should have no conflict of interest
- Death Certificate:
 - If you’ve attended a patient must issue a certificate or report to the coroner, if you are ‘available’
 - Are now able to sign for eg GP partner if you’ve reviewed notes and seen body
 - Different form for infants over 20 weeks gestation or > 400 gm and < 28 days old. Can be filled in by midwife
- Other forms:
 - Need an additional form before cremation, which is then cleared by the Medical Referee
 - Certificate of Life Extinct: police form to say the person is dead – eg if being referred to the Coroner. Does not include cause of death. Always take your own careful notes
- Changes following death:
 - Rigidity – ‘rigor mortis’. Linking of actin and myosin fibres following ATP depletion. Lasts from 6 – 8 hours after death to about 36 hours.
 - Lividity – blood seeps downwards – red congestion on downside of body
 - Temperature – indicator of time elapsed since death. Depends on temperature at death, BMI, clothing, etc
 - Decomposition
 - Rough guide to time of death:

Warm	Flaccid	< 3 hours
Warm	Stiff	3 – 8 hours
Cold	Stiff	8 – 36 hours
Cold	Flaccid	> 36 hours
- Homicide:
 - = Killing another, either directly or indirectly, or by accelerating death
 - Murder = intent to kill or cause serious injury or to facilitate another crime
 - Infanticide = death of child under 10 by a mother who has given birth or lactating
 - Can be hard to distinguish murder from suicide or accident in MVA, fire, drowning, or cot death

Coroner

- Has the status of a district court judge
- To initiate a coroner’s case, report the death to the police (who act as the coroner’s investigating agents)
- Must refer a death to the coroner if:
 - No known cause, suicide, unnatural or violent
 - No certificate issued
 - Died undergoing medical, surgical or dental procedure
 - Detained under A&D Act, committed or in prison
 - Child in CYPS or foster care
- Coroner can order an autopsy and/or hold an inquest
- Other court settings: District or High court
 - Expert witness can give an opinion, ordinary witness can only recount facts
 - Don’t take sides, be fair, stick to what you know, use notes taken on the occasion (with the permission of the judge)

Protection of Personal and Property Rights Act (1988)

- = PPPR Act

- Designed originally with intellectual handicap in mind. In acute or geriatric care, used mainly in cases of dementia
- Two underlying principles:
 - A person is competent until proven otherwise. Acts asserts right to autonomy, to refuse treatment and to manage their own affairs
 - Any order imposed shall be the least restrictive alternative. Encourages self-reliance, normalisation and community integration
- The judge has three decisions to make:
 - Determine jurisdiction
 - Determine whether an order needs to be made
 - Determine the type of order:
 - Enduring power of attorney (normally Powers of Attorney expire if the person becomes incompetent)
 - Welfare Guardian order (wholly lost capacity)
 - Property Manager order (wholly or partially lost capacity)
 - Personal order (wholly or partially lost capacity)
- 5 questions to assessing competency:
 - Does the person appreciate their situation
 - Can they understand the options that address their situation
 - Are they aware of the pros and cons of their choice
 - Do they express their choice clearly
 - Is their choice influenced by a distorted mind
- 6 stages in an application:
 - Consider clinical strategies
 - Assess competency
 - Complete application forms and a medical report
 - File application at family court
 - Family court appoints counsel
 - Pre-hearing conference, may lead to a full hearing

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Ethical Principles

- Beneficence: acting in a way that benefits the patient
- Paternalism: Substituting the doctor's judgement for that of the patient. The patient's autonomy is over-ridden. If the patient is not autonomous there is no paternalism. Can be justified or unjustified
- Non-maleficence: minimising harm. Harms should be outweighed by benefits
- Justice: fairness – all members of society share in its benefits and burdens
- Autonomy: ability to make one's own decisions. Exercising autonomy requires intellectual and emotional competence and the opportunity for action
- Dignity: preserving self respect, treating as a means not an end
- Truthfulness: central or absolute?
- Futility: endeavours that are doomed to failure. Depends on what the goal is

Morality and Standpoints

- Standpoints: law, religious belief, social conventions, morality – all give standpoints from which can define right and wrong – and they may disagree
- The scope of morality:
 - Self-imposed from within (cf. law – imposed form without)
 - Prescriptive: guides my action
 - Has universal character (moral principles don't always apply to everyone – but demand consistency in judgements)
 - But these things don't demarcate morality from other standpoints
- Bernard Gert: morality is a public system applying to all rational persons governing behaviour which affects others and which has the minimisation of evil as its end. I.e. it is an 'invention' for improving the human condition
- 4 competing concepts of ethics:
 - General principles impinging on human well-being
 - Principles providing a practical antidote to certain types of behaviour (e.g. those which exhibit limited sympathies) which impact on human well-being
 - Principles guiding the behaviour of a particular professional group (which makes a distinctive contribution to the human good)
 - Principles focusing on a particular dimension of human well being

Two Classes of Moral Theory

- Deontological: right/wrong due an essential feature of the behaviour – intrinsic
 - Excludes relevance of consequences
 - How do you work out what duties are – have to explain it in terms of intrinsic qualities
 - Kant is a prominent theorist: the principle (e.g. value of human life) embodied in an action makes an action a duty. End never justifies the means
- Teleological: right/wrong depending on whether it's a means to a good or a bad end – instrumental
 - Largest group is consequentialists of which utilitarianism is the most popular flavour
 - Utilitarianism: judge consequences by the greatest good for the greatest number
 - Must know consequences before you can judge it right or wrong
 - Is it limited to human happiness (what about animals)
- Both theories say liberty is important – but for different reasons

Confidentiality

- Hippocratic Oath: "Whatsoever things I see or hear concerning the life of men, in my attendance on the sick or even apart there from, which ought not to be noticed abroad, I will keep silence thereon, counting such things to be as sacred secrets"
- NZMA code of ethics:
 - Protects patients secrets even after death
 - Maintain confidence unless patient consents or required by law
- Benefits:
 - Access to information for the patient's benefit
 - Autonomy: patient control over information about them, respect for patient's choice
 - Dignity
 - Consequences: positive reinforcement of trust

- Legal requirements:
 - Health Information Privacy Code
 - Rule 10 (1): information obtained for one purpose cannot use that information for any other purpose
 - Rule 11(1): An agency must not disclose information unless...
 - Code of Health and Disability Service Consumer's Rights: Every consumer has the right to have his or her privacy respected
- Legal exceptions:
 - With patient's consent
 - Within the team of doctors caring for the patient. Not disclosed to students unless anonymised
 - Statutory e.g. Notifiable diseases, Land Transport Safety Authority (Driver's licence)
 - Disclosure in the public interest: Health Information Privacy Code allows disclose to prevent a 'serious and imminent threat'
 - Common Law: e.g. Tarasoff v Regents of the University of California case, Duncan v Medical Practitioners' Disciplinary Committee
- Special cases:
 - Children: does the child have the understanding and maturity to form a relationship of confidence
 - Incompetent adults: duty of confidentiality remains. The Health Information Privacy Code allows a representative of the patient to authorise disclosure
 - The dead: Patient's representative must authorise disclosure of information.
- Collection of health information discusses (Privacy code?):
 - Purpose e.g. necessary for a lawful purpose
 - Source: usually individual concerned
 - Collection: reasonable steps to ensure individuals aware of purposes, recipients and rights of access & correction
 - Manner: e.g. overly intrusive
 - Storage and security
 - Rights of access
 - Right for correction
 - Reasonable steps to ensure accuracy
 - Retention: not kept longer than required
 - Use limited to purpose for which it was collected
 - Limits on disclosure – breaching confidentiality:
 - Necessary to prevent/lessen serious and imminent threat to life/safety
 - Disclosure will lessen or prevent risk
 - Minimal information released compatible with preventing harm
 - Patient must be identified to reduce this risk
 - There is no better alternative
 - Recipient of the information can do something about it

Consent

- Function: to uphold and enhance the patient's autonomy – the right to think and act without coercion
- Code of HDS right 7: to make an informed choice and give informed consent except where any enactment of common law provides otherwise... (The code treats adults and children the same)
- Consent is a process of communication, openly gives information, honestly answers questions, in a setting and manner that the patient can understand
- Autonomy:
 - Requires the ability to form beliefs, make decisions, form preferences, form practical intent
 - Problems when these are completely or incompletely lacking, fluctuating, manifestly irrational
 - = A set of practical skills through which we make and act on decisions which accord with our own values
 - We should respect autonomy as this gives superior outcomes and because of underlying assumption that individual is best judge of his/her own good
- Requirements for consent:
 - Competence (ie autonomy)
 - Provision of information
 - Information is understood
 - Voluntary. Patient has control over the decision – ie lack of negative consequences, accustomed to obeying authority figures, feeling threatening by someone

- Individual must be able to understand that:
 - They have a choice (no coercion)
 - Why they are being offered treatment
 - What is involved
 - Probably benefits, risks, side effects, failure rates
 - Alternatives
- When you can't get consent:
 - Children lack legal capability to consent until 16. If patient under 16 doesn't want parents to know can't tell them.
 - If they are mentally or physically incapacitated
 - Can NOT use implied consent if the patient is incompetent – need consent of guardian, etc. But must treat in an emergency
- Presumption of competence: assumed competent until demonstrated otherwise (including children)
 - Varies with complexity of condition and treatment
 - Ask the patient! Do they understand why treatment is needed, what is involved, benefits, risks and alternatives
- **Children:**
 - Issue is not whether to get consent – but how
 - Inconsistency about when they are autonomous:
 - Guardianship Act: 16
 - Common Law (Gillick case 1985) and H&D code: Capacity to make decision
 - Exceptions to age limits and parental consent
 - Emergencies
 - Blood transfusion when life saving (if under 20 years)
 - Compulsory treatment (eg Mental health Act, Tb)
 - Blood alcohol
 - Abortion and contraception (CSA Act 1977): at any age, and no requirement to inform parents
 - Child Abuse examination (CYFS Act 1989)
 - When Guardianship invested in the Court or DG of Social Welfare
 - Good practice to involve the parents wherever possible
 - Consent and the UN Convention on the Rights of the Child
 - The best interests of the child are paramount (article 3)
 - Have the right to express their views and have them taken into account (article 12)
 - Privacy and Confidentiality (article 16)
 - Accessibility of information (article 17)
 - Conflict over consent:
 - Maori issues: greater expression of autonomy collectively, and collective responsibility for Tamariki. Involve whanau
 - If a child says no – it's usually because they are frightened. Take a child's views seriously. Reduce fear by ensuring understanding. But best interests may be in conflict with their wishes
 - If parents say no, consider reasonable alternatives and legal (last option). CYPS Act, sections 14 & 67 – child in need of protection. Guardianship Act 1968 may place child under guardianship of the court
 - Allow time to work it through, plan ahead
 - Avoid rushing important decisions
 - Give information, check it is understood, opportunity to ask questions
 - Enlist supports, Maori/PI staff, translator, etc
- **Consent in Research:**
 - Dates from Nuremberg trials → Declaration of Helsinki
 - Underlying principle: Concern for patient must be greater than the concern for science
 - Patient has same right to informed consent as with treatment

Compulsion

- Reasons for over-riding autonomy:
 - Autonomy is lacking: individual is no longer the best judge of his/her own good
 - Public well-being takes priority: autonomy present but over-ridden – well-being of others takes priority

- Paternalism: autonomy present (perhaps diminished) – prioritising the doctor's view of the patient's good over that of the patient
- Current legislation:
 - TB Act 1948: compulsory treatment
 - Health Act 1956: compulsory treatment of some infectious diseases
 - Alcohol and Drug Act 1966
 - Guardianship Act 1968: Dr can apply to make a child a ward of the court
 - CYPF Act 1989: some services parents can't refuse for their kids
 - Criminal Investigations Act 1995 and Land Transport Act 1998: compulsory taking of DNA/blood alcohol samples
 - Mental Health Act (Compulsory Assessment & Treatment Act) 1992 (See Compulsory Treatment, page 458)

Refusal of Treatment

- Refusing Consent:
 - Adults may refuse medical treatment even if it results in the person's injury or death (Section 11, Bill of Rights)
 - A pregnant woman may refuse treatment even if that jeopardises the life of her unborn baby
 - Not clear whether a competent child (under 20) can refuse treatment
 - Parents may refuse on behalf of children, except where refusal endangers the life of the child. Parent's right to practice religion etc does not extend to placing their child's health at risk
- Issues to consider:
 - Competence: are they 'autonomous'. Normal presumption is that they are, unless clear evidence to the contrary. Is the condition affecting their judgment? You can only have 'justified paternalism' where the person is autonomous. You are not being paternalistic where patient is incompetent.
 - The higher the level of risk, the greater need for evidence of competence (not just competence per se, but evidence of competence)
 - Informed consent: requires a competent person to voluntarily make a decision, who understands all the relevant information, including the doctor's recommendation.
 - Prognosis: if advanced terminal illness then this is different to where recovery is likely
 - Is the patient absent from coercion
 - Irreversibility of a decision not to intervene vs. reversibility of decision to intervene. Given this asymmetry, strong bias to intervention.
 - Weighing families wishes against patients
 - Loss of liberty and prolongation of misery if you intervene
- When is paternalism justified:
 - If intervention will probably prevent significant harm
 - Where benefits outweigh risks
 - Where the least autonomy restricting option that ensures the benefit is adopted
- Refusal of treatment on grounds of religious belief:
 - They still want treatment
 - Danger in accepting refusal to accept treatment at face value
 - Ensure understanding ('Why do you think this? Do you realise you are going to die without it?')
 - Ensure authenticity of beliefs (do they say they JW to avoid blood products they think are contaminated)
 - Identify acceptable treatment options
- Consequences of treating without consent:
 - Battery/assault
 - Breach of the patient's rights under the Bill of Rights/Code
 - Negligence
 - Disciplinary action

End of life issues

Euthanasia

- Euthanasia:
 - = Killing someone where, because of his or her distressing physical or mental state, this is thought to be in the person's own best interests
 - Voluntary euthanasia: killing a competent person, when that person requests it

- Non-voluntary euthanasia: assumed to be in the person's best interests – but they are not competent (eg babies, unconscious, mental incapacity)
- Involuntary euthanasia: against the person's will
- Arguments for euthanasia:
 - Autonomy and the right to die
 - Gives the person the choice to avoid pain and distress, loss of dignity, etc
- Arguments against:
 - Hazards of voluntary euthanasia in practice: fluctuating views, pressure from family
 - Life belongs to God
 - Intrinsic value of life
- Legal position is clear: doing anything to bring about death is murder, regardless of motive

Doctor Assisted Suicide

- If doctor gives the patient the means (eg leaves pills by the bed) then they have committed the offence of aiding and abetting suicide, punishable by up to 14 years imprisonment under s 179 of the Crimes Act
- Different from euthanasia as:
 - Doctor may not approve, but may respect the patient's choice
 - Clearer that the patient is making their own decision without coercion
- Reasons why doctors should be involved:
 - For:
 - They understand the medical condition (ie know the prognosis)
 - They are not an interested party (unlike families)
 - They know the best way of helping
 - Against:
 - They have a duty to preserve life
 - It might undermine confidence in the medical profession

Doctrine Of Double Effect

- It is wrong to perform a bad act even if there are good consequences
- It may be possible to do a good act, even if there may be bad consequences (eg giving pain relief knowing that it may hasten death)
- If the consequence is virtually certain, then it is considered 'intended' even if it wasn't the primary reason

Acts and Omissions

- Legally there is a distinction between doctors not doing something (ie failing to provide treatment) and doing something (ie giving a lethal injection). However, if the person has a legal obligation to act (eg a doctor), failing to do so may be culpable
- Doctors have a duty to provide the necessities of life to those under their care. Failing to do so is an offence under s151 of the Crimes Act. Considering medical treatment is not indicated, or that it is not in the patient's best interests, is a lawful excuse
- Ethically, omission is generally less bad than acts of commission

Withdrawal of life-sustaining treatment

- Is the patient competent – if so, the decision is the patient's. They have the right to refuse medical treatment under the bill of rights
- Incompetent patients:
 - Any advance directive?
 - Anyone authorised to make the decision on the patient's behalf (a guardian under the PPPR act or a formally appointed attorney). Patient's next of kin are *not* entitled to consent on a patient's behalf
 - Decisions about whether treatment serves no therapeutic purpose are a medical decision (although see section 7(4) of code of rights re informed consent). There is no duty to continue with life-sustaining treatment where there is no prospect of recovery or any quality of life
 - Should discuss with family
 - Discuss with colleagues (safety in numbers)
- Cause of death will be the underlying cause, not the withdrawal of treatment
- Withdrawal will be treated as an omission, not an act. Courts have ruled there is no difference between turning the ventilator off and not turning it on to start with

- Rules of thumb:
 - Intention is always to act in the patient's best interests
 - Err on the side of caution. Always get a second opinion. If in doubt, seek a court judgement

Advance Directives

- Every competent patient has the right to refuse treatment, even if this leads to his or her death. This includes the right to leave clear instructions in case they may be incompetent in the future \Rightarrow an advance directive. Recognised in the Bill of Rights
- A directive is valid if:
 - The patient was competent at the time it was made
 - They were free from undue influence
 - They were sufficiently informed
 - They intend their directive to apply to circumstances which subsequently arise
- These conditions should be tested at the point where a directive is applied

Ethical Issues in Dealing with Impaired or Incompetent Colleagues

- Summary:
 - Collective responsibility as important as individual
 - Maintenance of public trust vital
 - Better team work and error reporting will help
 - Self regulation: use it or lose it
- Issues:
 - Trust of patients in doctors: patients in vulnerable position
 - Beneficence
 - Legal requirement to report impaired or incompetent doctor
 - Collective responsibility: to patient population as a whole
 - Uncertainty: may explain but not excuse failure to act
 - Professional etiquette (often disguised as 'clinical freedom') – not wanting to interfere in other's livelihoods
 - Loyalty to the group: key to cooperation but should be overridden by maleficence
 - Pattern of error not a single mistake is indicative of incompetence
- Criteria for whistle-blowing:
 - Evidence of severe harm
 - Good chance of reducing harm
 - All other avenues explored
- Ethical institutions
 - Encourage reporting of error (ie about safety not culpability)
 - Mechanisms for self/peer assessment
 - Internal complaints mechanisms (with protection)
 - Guard against malicious complaints
- Culture within a group:
 - Less competent influencing each other
 - Professional isolation (big risk factor for incompetence)
- Hard to pin down doctors because:
 - Lack of benchmarking (little medical practice has been validated)
 - Clinical freedom
 - 'Half of all doctors are below average'
 - The learning curve: period of necessary and acute incompetence
- Informed consent: what is it reasonable for patients to know about their doctors (eg individual success rates) vs. doctors right to privacy

Professional Ethics

- Characteristics of a profession: an important service, monopoly, self regulating, extensive training with intellectual component, autonomy in work
- Professional ethics:
 - Ethics and values in roles and conduct of professionals
 - Aspirational and regulatory component
 - Ethics should reflect common social values: freedom, protection, equality, privacy, etc

- Obligations to patients:
 - Previously paternalism
 - Then contractual model (but didn't acknowledge power imbalance)
 - Fiduciary model – built on trust – Doctor makes a recommendation, patient has informed consent
- Values:
 - Honesty – eg conflict of interest
 - Competence
 - Diligence – give sufficient time and effort to the patient
 - Loyalty and objectivity
 - Fairness
 - Discretion
 - Professionals as employees: issues around obligation to obey vs autonomy, whistle blowing, strikes
- Economic issues: fee splitting (eg taking a cut out of a referral), accepting gifts, limits on advertising
- Professional self-regulation: admitting, setting and applying norms

Tissue Donation

- Problems of supply:
 - Fair distribution (resource allocation)
 - Dead bodies:
 - When are they dead (brain death criteria, PVS, anencephalic infants)
 - Who gives consent, family distress vs need for a quick decision
 - Should there be a presumption of donation (with right of opt out) – small constraint on freedom outweighed by significant benefit?
 - Live bodies:
 - Increased supply
 - Operative and consequent risks for donor
 - Consent (especially if donor is a child or non-competent adult)
 - Donor/recipient relationship as source of pressure
 - Buying and selling:
 - Increase supply
 - Objections: Consent (free and informed?), exploitation, degradation, misinformation
 - Fetal tissue:
 - Increases supply
 - Fewer rejection problems
 - Sourced from abortion
 - ‘Surplus’ embryos
 - Animal Tissue
- Regulation:
 - Health Act 1956 controls donation and prohibits profit making
 - Human Tissue Act 1964 regulates organ removal after death – mixed opting in/opting out arrangement
 - Living Donors: common law – unlawful to remove a body part if not therapeutic for the donor [Blood is covered by the Health Act]

Assisted Human Reproduction

- 3 types:
 - Couples using their own genetic material
 - Techniques using other people's genetic material
 - Techniques using another women's womb (surrogacy)
- Current issues:
 - Surrogacy – non-commercial IVF
 - Posthumous use of sperm (creation of fatherless families)
 - Should women have access to IVF if they already have children (eg following tube reversal) – is there a fair innings?
 - Intergenerational gamete donation (assisted incest!)
 - Pre-implantation genetic diagnosis (PGD)
 - To what extent should families be free to make their own choices

- The significance of life
- Does PGD devalue affected individuals
- What is the meaning of disability
- Who will have access to these diagnostic techniques
- Ethical issues:
 - Human dignity, the value of life and what it is to be human
 - Autonomy
 - Procreative liberty vs the role of the state (reflecting the welfare of society)
 - Informed consent – eg pressure on surrogate mums
 - Beneficence:
 - Who benefits
 - What are the best interests of the child not yet conceived. They should be an end in themselves, not a means to someone else's end
 - Non-maleficence (do no harm)
 - Commodification of children
 - Incrementalism – the ‘slippery slope’
 - Unknown/possible harms – Intra-cytoplasmic sperm injection has become common without any long term trials looking for any effects on kids
 - Justice
 - Fair access to AHR procedures
 - Prioritisation of need and benefit
 - Infertility vs social reasons (eg post vasectomy, freezing eggs till after you've had a career, etc)

Innovative Treatment

- Ethics committees must review research and innovative treatments
- The difference:
 - Research is for the benefit of society and future patients
 - Treatment is for the benefit of the patient
 - Innovative practice sites between these
- Defn: Innovative treatment is those procedures which are new to a particular provider setting in NZ, or which are being used for a new purpose (Has often been harmful, at a minimum it introduces greater or new risk of harm)
- 3 issues:
 - Proving they are safe and effective. Issues here vary – if it is an established technique overseas the issue is whether the NZ practitioners are and will remain competent. If it's entirely new, is it safe? Etc. Proving safety is difficult in surgical procedures – the surgeon is gaining skill, case comparison is complicated, random allocation may be unethical. Safety should be established early on. Effectiveness should be assessed in a way that gives good statistical evidence
 - Gaining informed consent to non-standard treatment
 - Defining what constitutes an innovative procedure

Research Ethics

- Codes:
 - Nuremberg code:
 - Informed consent of subjects, and liberty to withdraw
 - Benefits to society (can't be got by other means)
 - Avoid unnecessary suffering and injury
 - Degree of risk not greater than potential benefit of problem to be solved
 - Only conducted by scientifically qualified persons
 - Declaration of Helsinki: 1964, revised 1975. Main difference: required to be supervised by medically qualified person
- Experiments on people that won't benefit current patients
 - If study not sound then won't answer questions ⇒ risk not worth it and waste of resources
 - Informed consent by participants
 - Ensure study remains ethical in progress ⇒ ‘stop’ criteria and monitoring of interim results
 - ‘Therapeutic Research’ a misnomer (although used in Declaration of Helsinki). In research, if the patient happens to benefit that's coincidental. Research subject gives up normal expectation of tailored treatment.

- Placebos:
 - ‘Equipoise’: randomisation only ethical if there is justifiable uncertainty of merit between intervention and control – but reasonable possibility that the new treatment is better than placebo
 - Must be significant knowledge to be gained from a placebo trial
- Implications of randomisation
 - Severs normal connection between patient and individually tailored treatment
 - Must be able to break the code if things don’t go as expected
- Investigator requirements:
 - Competence
 - Moral Character? Hard to specify or enforce
 - Conflicts of interest:
 - Intrinsic: interested in gaining knowledge verses care for the patient
 - Extrinsic: funding, reputation
 - Clinical equipoise
- Balancing harms and benefits:
 - Principle of non-maleficence
 - Healthy problems: only very small risk acceptable. Problem of financial inducements (attract people to take too much risk?)
 - Extrapolation from healthy volunteers not always possible
- Equitable subject selection:
 - Respect for people (informed consent)
 - Principle of justice (equal sharing of benefits and burdens)
 - Vulnerable groups: reduced capacity to protect their own interests: eg incompetent, dying, minority groups, 3rd world countries (but nothing in ethical codes to preclude their use – justification becomes harder as degree of risk and degree of vulnerability increases)
- Therapeutic orphans:
 - = Drugs not licensed for some groups, eg:
 - Children: difficulties of doing research on children. So package says “not recommended” → informed consent issues for the doctor and patient
 - Women: pregnancy and lactation, financial implications of teratogen testing
- Problems with informed consent:
 - People often don’t easily understand things like randomisation
 - People often reticent to ask questions
- Role of Ethics Committees:
 - No statutory requirement for ethical review – but defacto requirement
 - Composition: Lay chairperson, 50% lay membership (following Cartwright)
 - Should journals publish research that hasn’t undergone ethical review:
 - For: if its sound, would deprive society of valuable information and would require the study to be repeated
 - Against: journal editors should be ethical gatekeepers
- Problems with Prof Greens cervical cancer experiment:
 - Poor study design but still approved
 - Consent not gained from patients
 - Study not monitored properly (should have been stopped due to evidence of harm)
 - Concerns of other doctors not acted on properly
- Questions it raises:
 - To whom should the doctor be accountable: their own conscience, patients or colleagues
 - Women were vulnerable, being examined by men ⇒ asymmetry of power exaggerated

Cram Cards

<u>Causes of Acute Sinusitis</u> Strep pneumoniae H influenzae [Also B catarrhalis and Strep pyogenes]	<u>Causes of Acute Infectious exacerbations of Chronic Bronchitis</u> Strep Pneumoniae H Influenzae Branhamella Catarrhalis	<u>Causes of Otitis Media</u> Strep Pneumoniae H Influenzae Branhamella Catarrhalis
<u>Urinary Tract Infections</u> Usually E. Coli. Treatment: <ul style="list-style-type: none">1st line: Oral Trimethoprim (effective against community acquired E Coli, Klebsiella, Proteus, Strep faecalis)2nd line: Oral Quinolones (eg Norfloxacin)Single dose therapy less effective	<u>Causes of Acute Pharyngitis</u> <ul style="list-style-type: none">Viral (commonest): Rhinovirus, coronavirus, Influenza A & B, Parainfluenza 1 – 3, Adenovirus, Herpes Simplex, EBVBacterial: Strep Pyogenes (Gp A), Strep Group C, Mixed anaerobes (gingivitis – poor dental hygiene), Corynebacterium diphtheria, Neisseria gonorrhoeaeFungal: Candida Albicans	<u>Adenovirus</u> Sore throat (erythema + maybe exudate even though a virus), fever, headache, myalgia, <i>conjunctivitis</i>
<u>Aspergillus</u> <ul style="list-style-type: none">A saprophytic hyaline mould – lives on dead organic matterHaemorrhagic pneumonia in immunocompromised (incl. acute leukaemia)Treatment: Amphotericin B. Itraconazole for prophylaxis	<u>Bacteroides Fragilis</u> <ul style="list-style-type: none">G+ive anaerobic bacilli. Dominant gut microbeCauses: abdominal wound sepsis, peritonitis, pelvic sepsis, septic abortion, puerperal sepsis, any abscess incl. brain abscess from otitis media or haematogenous spreadTreatment: Metronidazole (<i>not</i> penicillin)	<u>Bordetella Pertussis</u> <ul style="list-style-type: none">Causes whooping coughCough followed by inspiratory gasp (whoop), apnoea, vomitingCan → encephalitis. 50% of < 6 months get admittedIncidence: up to 5000 cases a yearTreatment: Erythromycin
<u>Candida Albicans</u> <ul style="list-style-type: none">Yeast causing white plaques↑ Infection in immunocompromised, steroid use or long term antibiotics Treatment: <ul style="list-style-type: none">Topical: NystatinOral: Terbinafine for scalp or nailsSTD: Clotrimazole pessarySevere: Fluconazole (good CSF penetration) or Amphotericin B (good but nasty side effects)	<u>Campylobacter Jejuni</u> <ul style="list-style-type: none">G+ive rodTreatment: Erythromycin (used to be ciprofloxacin [a quinolone] but it's been put in chicken feed → ↑resistance)	<u>Chlamydia Trachomatis</u> <ul style="list-style-type: none">Obligate Intracellular bacteriaRarer cause of pneumonia (farm animals). Tx: erythromycin (has penicillinase) STD (types D – K):<ul style="list-style-type: none">Incubation 7 – 21 days. Need Endocervical sampleDoxycycline 7 days or Azithromycin stat. Pregnancy: Erythromycin (to avoid PROM). PID: Doxycycline/ erythromycin + ornidazole (antianaerobe like metronidazole)Reiter's syndrome (autoimmune): arthritis + urethritis + conjunctivitis
<u>Clostridium</u> <ul style="list-style-type: none">G+ive anaerobe, spore formingC Perfringens: Abdo wound sepsis, peritonitis, pelvic sepsis, puerperal sepsis, gas gangrene (clostridial myonecrosis), food poisoning (Enterotoxic)C TetaniC BotulinumC Difficile: Pseudomembranous colitis following antibiotics, anaerobe. Tx: Metronidazole (2nd line Vancomycin)	<u>Cytomegalovirus (CMV)</u> <ul style="list-style-type: none">Transmission: saliva, blood, organ donationImmunocompetent:<ul style="list-style-type: none">Kids: asymptomaticAdults: self-limiting – maybe fever for 2 weeksPregnancy: Congenital infection in 20 – 40%. Occasional long term sequelae (deafness, retardation, respiratory distress)AIDS: retinitis common, rarely encephalitis & colitisOrgan transplant: Interstitial pneumonia, hepatitisTx: Ganciclovir	<u>Coliforms (= G+ive bacteria)</u> <ul style="list-style-type: none">Incl. E. Coli + Klebsiella + Proteus mirabilisCause UTIs, Pyelonephritis, abdo wound sepsis, peritonitis, biliary tract infection Tx: <ul style="list-style-type: none">Meningitis & brain abscess: 3rd gen Cephalosporin – good CSF penetration (Cefotaxime, Ceftazidime). Consider also Gentamicin & Cotrimoxazole
<u>Corynebacterium Diphtheriae</u> <ul style="list-style-type: none">G+ive bacilliCauses diphtheriaRare now (1 NZ case in last 20 years)Sore throat, fever, pain on swallowing, headache, vomiting, grey/green exudate on pharynxToxin → cardiac & neuro toxicity	<u>Cryptococcus Neoformans</u> <ul style="list-style-type: none">Yeast with mucinous capsuleIndian ink stain +iveCauses encephalitis in AIDS, Pneumonia & aseptic (=lymphocytic) meningitis in immunocompromisedTx: Fluconazole or Amphotericin B	<u>Cryptosporidium</u> <ul style="list-style-type: none">Common protozoan parasiteProfuse watery diarrhoeaDiagnosis: stool microscopy (ZN stain for acid fast cysts)No effective antibiotic treatment (can try Paromomycin – oral, nonabsorbable aminoglycoside)
<u>E Coli</u> <ul style="list-style-type: none">G+ive rods. A coliform. Grows on MacConkey agarMost are harmless bowel commensals but can → peritonitis (burst appendix), cystitis, neonatal meningitisTx:48% resistant to amoxicillin. Augmentin resistance growingGentamycin or Trimethoprim	<u>Epstein Barr Virus</u> <ul style="list-style-type: none">Respiratory spread, usually young adultsSore throat (erythema/exudate in 50%), fatigue, malaise, fever, headache, posterior cervical lymphadenopathy, splenomegaly, hepatitis, atypical mononucleosisDon't give penicillin → rash mistaken for allergyDiagnosis:After 7 days Anti-EBV IgM (lasts 2-4 months) and IgG (lasts for life)After 2 months EBNA (lasts for life)	<u>Enterococcus Faecalis</u> <ul style="list-style-type: none">AeroCauses UTI, abdominal wound sepsisTx: Amoxycillin (not penicillin G)

Otitis Media

**Acute Infectious Exacerbations
of Chronic Bronchitis**

Acute Sinusitis

Adenovirus

Acute Pharyngitis

Bladder Infections (UTIs)

Bordetella Pertussis

Bacteroides Fragilis

Aspergillus

Chlamydia Trachomatis

Campylobacter Jejuni

Candida Albicans

Coliforms

CMV

Clostridium

Cryptosporidium

Cryptococcus Neoformans

Corynebacterium Diphtheriae

Enterococcus Faecalis

EBV

E Coli

<p><u>Gardnerella Vaginalis</u></p> <ul style="list-style-type: none"> Causes Bacterial Vaginosis Symptoms: greyish-white, smelly discharge Clue cells on Gram stain Crowds out Lactobacilli Tx: Anti-anaerobe: Metronidazole (oral and/or pessaries) 	<p><u>Haemophilus Influenzae</u></p> <ul style="list-style-type: none"> G -ive bacilli Type A: Causes acute otitis media, sinusitis, infections, exacerbation of chronic bronchitis, pneumonia in chronic lung disease, rarely meningitis (\rightarrow 3rd gen Cephalosporin – ↑CSF pen) Tx: 6% resistant to penicillins, not sensitive to erythromycin \Rightarrow cefaclor, cefuroxime (iv), ceftriaxone, augmentin, tetracycline (not kids/pregnant) Type B: causes epiglottitis in kids 	<p><u>Herpes Simplex 1 & 2</u></p> <ul style="list-style-type: none"> Incubation 2 – 25 days Type 1: face, use zovirax cream. Also STI. Type 2: STI. Prevalence 20%. Tx Acyclovir Encephalitis: confusion, convulsions. PCR test of CSF. Give acyclovir on suspicion Pharyngitis: Mild \rightarrow like other URTI. Severe \rightarrow exudate/erythema, shallow ulcers, vascular rash on lips
<p><u>Helicobacter Pylori</u></p> <ul style="list-style-type: none"> G -ive rod, curved/spiral shaped Urease breath test: swallow C13 labelled Urease, expire C13 labelled CO2 Investigations: CLO test, biopsy, micro, serology Prevalence 30% but declining Causes gastritis (usually asymptomatic) In 70-80% of gastric ulcers, 95% of duodenal ulcers Triple therapy: eg clarithromycin + metronidazole + omeprazole (\rightarrow ↑pH \rightarrow ↑antibiotic bioavailability) 	<p><u>Influenza A & B</u></p> <ul style="list-style-type: none"> Causes flu: common cold + fever, headache, generalised myalgia; most common cause of viral pneumonia 400 deaths per annum Vaccinate each year for new strains due to antigenic drift 	<p><u>Listeria Monocytogenes</u></p> <ul style="list-style-type: none"> G +ive bacilli Tx: amoxycillin Neonatal meningitis Elderly/immunocompromised: Tx ciprofloxacin (a quinolone – not in kids)
<p><u>Legionella</u></p> <ul style="list-style-type: none"> Pneumonia: fibro-purulent exudate in 40 – 70 year old smoker. Slow onset, headache, delirium, ?more GI effects Tx: erythromycin (has penicillinase) + rifampicin if severe 	<p><u>Mycoplasma</u></p> <ul style="list-style-type: none"> Common cause of URTI Pneumonia: benign, self-limiting, age 5 – 15 <p>Tx:</p> <ul style="list-style-type: none"> Erythromycin 2nd line: Tetracyclines (eg doxycycline) except pregnant/kids Resistant to Augmentin 	<p><u>Measles</u></p> <ul style="list-style-type: none"> Interstitial pneumonia in immunocompromised kids
<p><u>Moraxella Catarrhalis</u> <u>(=Branhamella Catarrhalis)</u></p> <ul style="list-style-type: none"> Causes: acute otitis media, acute sinusitis, acute infectious exacerbation of chronic bronchitis, pneumonia in chronic lung disease Tx: 70% has penicillinase \Rightarrow augmentin, cefaclor, tetracycline, cefuroxime 	<p><u>Neisseria Gonorrhoea</u></p> <ul style="list-style-type: none"> G-ive diplococci, bean shaped, hard to culture (chocolate agar), survives intracellularly STD incubation: 1 – 14 days Male: discharge and dysuria. Female: only 20% symptomatic \rightarrow PID <p>Tx:</p> <ul style="list-style-type: none"> Stat: Amoxycillin + Probenecid Ciprofloxacin (quinolone) or tetracycline (eg doxycycline) if penicillin allergy or resistant Azithromycin if concurrent chlamydia or pregnant 	<p><u>Neisseria Meningitidis</u></p> <ul style="list-style-type: none"> G -ive diplococci (bean shaped). Liberated endotoxin Kids & adults meningitis, <i>not</i> otitis media Notifiable disease Tx: Penicillin, Cefotaxime if allergic Prophylaxis: Rifampicin (broad spectrum), ceftriaxone if pregnant
<p><u>Parainfluenza virus (1-3)</u></p> <ul style="list-style-type: none"> Causes Croup (laryngotracheobronchitis) Initial: sore throat, rhinorrhoea, mild cough Leads to: sever cough (seals bark), hoarseness, inspiratory stridor (subglottic inflammation) 	<p><u>Pneumocystis Carinii Pneumonia</u></p> <ul style="list-style-type: none"> Extracellular protozoan parasite Exclusively infects the lung, mainly in AIDS (also transplant, leukaemia) Tx: Cotrimoxazole (=trimethoprim +sulphamethoxazole) Relapse common 	<p><u>Pseudomonas aeruginosa</u></p> <ul style="list-style-type: none"> G -ive rod. Low virulence but antibiotic resistance. Grows in anything Common in burns, immunocompromised and CF Causes haemorrhagic pneumonia <p>Tx:</p> <ul style="list-style-type: none"> Increasing resistance. Always to sensitivities Meningitis: Ceftazidime Ciprofloxacin (Quinolone) – its main use Tobramycin (Aminoglycoside) or piperacillin
<p><u>Respiratory Syncytial Virus</u></p> <ul style="list-style-type: none"> Major cause of URTI, esp winter/spring Starts as URTI (cough, fever, sore throat) \rightarrow LRTI (mainly bronchiolitis) with dyspnoea, tachypnoea Tx: If severe then Ribavirin aerosol 	<p><u>Rhino Virus and Coronavirus</u></p> <ul style="list-style-type: none"> Common cold Fever uncommon except in kids 	<p><u>Staph Epidermidis</u></p> <ul style="list-style-type: none"> G +ive, Coagulase -ive Causes infected Hickman line, IV lines (esp neonates) Less virulent than Staph Aureus Tx: Flucloxacillin (one EMPTY stomach). If resistant then Vancomycin
<p><u>Staph Aureus</u></p> <ul style="list-style-type: none"> G +ive, Coagulase +ive (fibrinogen \rightarrow fibrin) Causes: mastitis, diabetic foot infections, furuncles (if recurrent then ?nasal carriage \rightarrow rifampicin), infected lines, hospital acquired pneumonia, abscess, endocarditis, food poisoning (esp in cream), osteomyelitis Tx: Flucloxacillin. Allergy: Ceftriaxone. MRSA (resistant to flucloxacillin and cephalosporins): Vancomycin (also quinolones) 	<p><u>Strep Pneumoniae</u></p> <ul style="list-style-type: none"> G+ive diplococci, α haemolytic Causes: acute otitis media, sinusitis, community acquired pneumonia, infectious exacerbation of chronic bronchitis, meningitis Oral: amoxycillin. IV: Penicillin G (1% adults resistant, 10% kids). Allergy: erythromycin (not for meningitis, poor CSF penetration) Penicillin resistant: Ceftriaxone (3rd gen) or Vancomycin. Resistant and Meningitis: Cefotaxime. Resistant and Endocarditis: Vancomycin 	<p><u>Syphilis</u></p> <ul style="list-style-type: none"> Caused by Treponema pallidum \rightarrow ↓Lumen of small arteries due to ↑intima Primary: chancre – painless hard macule at site of sexual contact. Secondary: 4 – 8 wks later, fever, malaise, lymphadenopathy, rash, alopecia Tertiary: latent for 2 – 20 yrs, gummas (granulomas), ascending aortic aneurysm, aortic regurgitation, cranial nerve palsies, dementia Diagnosis: serology (VDRL test). Tx: Penicillin G (im). If resistant then tetracyclines (eg doxycycline)

Herpes Simplex 1 & 2

Haemophilus Influenzae

Gardnerella Vaginalis

Listeria Monocytogenes

Influenza A & B

Helicobacter Pylori

Measles

Mycoplasma

Legionella

Neisseria Meningitida

Neisseria Gonorrhoea

Moraxella Catarrhalis

Pseudomonas aeruginosa

**Pneumocystis Carinii
Pneumonia**

Parainfluenza Virus 1 - 3

Staph Epidermidis

Rhino Virus and Coronavirus

Respiratory Syncytial Virus

Syphilis

Strep Pneumoniae

Staph Aureus

<p><u>β Haemolytic Strep Group B</u></p> <ul style="list-style-type: none"> • β Haemolytic = clear on blood agar • Eg Strep agalactiae (vaginal flora). [NB Strep pyogenes in β haemolytic Lancefield Group A] • Causes: meningitis, respiratory distress syndrome • Tx: Penicillin 	<p><u>Strep Pyogenes</u></p> <ul style="list-style-type: none"> • β haemolytic, Lancefield Group A. G +ive singly or in chains • Common cause of cellulitis, pharyngitis, impetigo • Can → Rheumatic fever & glomerulonephritis • Tx: Penicillin (little resistance) • Erythromycin if allergic • Not amoxycillin unless Pyogenes is proven – if virus → rash which is mistaken for allergy 	<p><u>Viridians Strep</u></p> <ul style="list-style-type: none"> • = α haemolytic (green on blood agar). G +ive • Eg Strep Sanguis • Causes: UTI, wound sepsis • Infective endocarditis: Tx: penicillin or amoxycillin +/- gentamycin (for G –ive cover)
<p><u>TB</u></p> <ul style="list-style-type: none"> • Mycobacterium Tuberculosis • Waxy coat resists lysis after phagocytosis → granulomas. Infects anything (lung, lymph nodes, brain, gut) • Acid fast bacilli – use ZN stain • Tx: Rifampicin + isoniazid + pyrazinamide (also ethambutol) • In AIDS, consider M avium intracellulare. Resistant to Tb drugs. Consider Clarithromycin 	<p><u>Trichomonas</u></p> <ul style="list-style-type: none"> • Causes Trichomoniasis • Watery green/yellow fishy smelling vaginal discharge • Protozoa • Common 3rd world STD • Tx: Doxycycline, metronidazole 	<p><u>Varicella Zoster</u></p> <ul style="list-style-type: none"> • Chicken pox. • Latent in dorsal root ganglia → shingles • Culture possible if transported in viral medium • Tx for shingles: • Acyclovir as early as possible • Analgesic or low-dose amitriptyline for pain
<p><u>Toxoplasmosis</u></p> <ul style="list-style-type: none"> • Protozoa/parasite. In meat cysts (and kitten faeces) • Causes: lymphadenopathy (eg unilateral), maybe fever, myalgia, acute pharyngitis, hepato-splenomegaly, atypical mononucleosis, takes while to settle. AIDS: CNS involvement, retinal lesions • Congenital: Prem, still birth, choroido-retinitis, (worse in 3rd trimester) • Lab: PCR of amniotic fluid, CSF. Serology: IgM peaks at 2-4 weeks, traces for up to a year • Tx: Pyrimethamine+clindamycin, Pregnant: Spiramycin 	<p><u>Malaria</u></p> <ul style="list-style-type: none"> • Irregular fever, headache, malaise, vomiting (like typhoid). Lab: Blood film <i>when febrile</i>. Chemoprophylaxis • Mefloquine weekly: good against chloroquine resistant Falciparum. Not if epilepsy, pregnant, babies • Doxycycline daily: Esp in SE Asia (mefloquine-resistant Falciparum). Not kids or pregnant • Chloroquine + Proguanil: Only one safe if pregnant • Chloroquine weekly (if no chloroquine-resistant falciparum eg Central America) 	<p><u>Plasmodium Falciparum</u></p> <ul style="list-style-type: none"> • No reinfection, cerebral malaria, Africa • Quinine sulphate + Doxycycline 7 days • Cerebral malaria: IV quinine
<p><u>Plasmodium Vivax</u></p> <ul style="list-style-type: none"> • Asia/Oceania, exo-erythrocytic liver cycle • 3 days of Chloroquine • Radical cure (P Vivax or P Ovale): Primaquine 2 weeks (test for G6PD deficiency first) • Relapse common → 3 days chloroquine then higher dose of primaquine 	<p><u>Giardiasis</u></p> <ul style="list-style-type: none"> • Explosive, watery diarrhoea • Stool exam, 3 samples, 48 hours apart → trophozoites • Tx: Tinidazole stat or Metronidazole 7 days • Relapse not uncommon 	<p><u>Amoebiasis</u></p> <ul style="list-style-type: none"> • Lab – look for cysts. • May be extra-intestinal (eg abscess) → antibody test • Metronidazole + diloxanide furoate
<p><u>Filarisis</u></p> <ul style="list-style-type: none"> • Eg Wuchereria Bancroft • → Elephantitis. May need Surgery to relieve blocked lymphatics • Tx: Ivermectin 	<p><u>Intestinal Worms</u></p> <ul style="list-style-type: none"> • Hookworm, roundworm, pinworm: Medendazole (treat whole family) • Strongyloides Stercoralis: Thiabendazole • Tapeworms: Niclosamide 	<p><u>Travel Medicine</u></p> <ul style="list-style-type: none"> • Malaria: prophylaxis if > 7 days. Risk in resort areas low • Hep A: Usually given • Typhoid: injectable or oral vaccine • Yellow fever: equatorial Africa & South America • Polio, tetanus and diphtheria • Meningococcal (Types A,C,W,Y): Nepal, West Africa, Brazil • Japanese Encephalitis: SE Asia. Rare for travellers to get it
<p><u>Cephalosporins</u></p> <ul style="list-style-type: none"> • 1: Cefazolin: Better for G+ (not E faecalis) and anaerobes (not B fragilis) • 2: Cefuroxime: Better against Coliforms. Active against H influenzae • 3: Ceftriaxone, Cefotaxime: Good against most coliforms. Not Bacteroides or Enterococcus. Good CSF penetration. • 4: Cefipime: Good for β-lactamases, coliforms & pseudomonas 	<p><u>Macrolides</u></p> <ul style="list-style-type: none"> • Good against streps, mycoplasma, chlamydia or legionella pneumoniae, Campylobacter • Not H influenzae • No CSF penetration • Chlamydia trachomatis in pregnancy • Erythromycin, Roxithromycin (Rulide), Clarithromycin (for MAC), Azithromycin (Stat, for Chlamydia or Gonorrhoea STDs in pregnancy) 	<p><u>Vancomycin</u></p> <ul style="list-style-type: none"> • Only active against G+ • Systemic MRSA/MRSE infection • Staph or Strep Endocarditis with penicillin allergy • C Difficile colitis (oral) – use Metronidazole first • Otto and nephrotoxic
<p><u>Rifampicin</u></p> <ul style="list-style-type: none"> • Always in combination (except meningitis and Hib prophylaxis) • Tb, Severe staph or legionella infection 	<p><u>Aminoglycosides</u></p> <ul style="list-style-type: none"> • Active against all coliforms, pseudomonas • Inactive against strep, anaerobes • For G- sepsis, perforated appendix • Otto and nephro toxic 	<p><u>Cotrimoxazole</u></p> <ul style="list-style-type: none"> • = Trimethoprim + sulphamethoxazole • Broad spectrum • For acute infectious exacerbations of chronic bronchitis, PCP • Trimethoprim only for community acquired UTI (so those with sulphur allergy can use)

Viridians Strep

Strep Pyogenes

β Haemolytic Strep Group B

Varicella Zoster

Trichomonas

Tb

Plasmodium Falciparum

Malaria

Toxoplasmosis

Amoebiasis

Giardiasis

Plasmodium Vivax

Travel Medicine

Intestinal Worms

Filariasis

Vancomycin

Macrolides

Cephalosporins

Cotrimoxazole

Aminoglycosides

Rifampicin

<u>Quinolones</u>	<ul style="list-style-type: none"> • Broad spectrum (except anaerobes and streps) • Not in kids (damages growth cartilage) • Norfloxacin: resistant UTIs • Ciprofloxacin: Pseudomonas 	<u>Tetracyclines</u> <ul style="list-style-type: none"> • Eg Doxycycline • Active against staph, streps, coliforms, HIB • Used in STDs • Syphilis and Gonorrhoea if penicillin allergy • Mycoplasma pneumoniae • Not in pregnancy or kids < 12 (stains teeth and deposits in bone) 	<u>Metronidazole</u> <ul style="list-style-type: none"> • Active against all anaerobes (eg B fragilis) • Inactive against aerobes (except Gardnerella Vaginalis – drug of choice) • Active against protozoa: eg Giardia
<u>Antifungals</u>	<ul style="list-style-type: none"> • Nystatin (topical): vaginal/oral candida • Miconazole (topical): Candida and dermatophytes (except scalp and nails) • Terbinafine (oral): dermatophytes of scalp and nails • Fluconazole (oral/iv): Yeasts (candida, cryptococcus). Good CSF penetration • Itraconazole (oral): Dermatophytes of scalp & nails, candida/aspergillus prophylaxis in AIDS • Amphotericin B (iv): very good but nephrotoxicity 		

Metronidazole	Tetracyclines	Quinolones
		Antifungals

<p style="text-align: center;"><u>Back Exam</u></p> <ul style="list-style-type: none"> • Walk: gait, walk on toes (S1), walk on heels (L5, ie neuro signs) • Look: <ul style="list-style-type: none"> • Is belt line horizontal • Skin: Scars, pigmentation • Shape & Posture: if scoliosis then bend over • • Palpate: <ul style="list-style-type: none"> • Spinous processes (support forehead for neck) for tenderness or a step • Sacroiliac joint • • Move: <ul style="list-style-type: none"> • Neck: flexion, extension, rotation, lateral flexion • Back: <ul style="list-style-type: none"> • Flexion: Schober's test • Extension • Lateral Flexion • Rotation (sitting on a chair) • • Special tests: <ul style="list-style-type: none"> • Check neurology in arms and legs if neck or lumbar pain (Sciatic pain – Lasegue's test, power, tone, reflexes, sensation, co-ordination) • Do abdominal exam if lumbar pain (eg AAA) 	<p style="text-align: center;"><u>Hip Exam</u></p> <ul style="list-style-type: none"> • Standing: <ul style="list-style-type: none"> • Gait • On toes (S1), on heels (L5) (checking neurology) • Bend over – how can they reach (examine back) • Crouch down (test knees and extensor mechanism) • Observe: gluteus bulk, posterior scars • Trendelenburg test and sacroiliac joint • • Look: <ul style="list-style-type: none"> • Skin: scars, redness • Soft tissue: swelling • Muscle: wasting – quads, abductors, adductors • Bony deformity • Apparent and real leg length • • Feel: <ul style="list-style-type: none"> • Groin: hernias, lymph nodes • Greater trochanter tenderness → ilio-tibial band pain • • Move (compare sides): <ul style="list-style-type: none"> • Thomas test: fixed flexion deformity • Flexion (comparing sides) • Adduction and abduction with pelvis fixed • Internal and external rotation (comparing sides) • Exam knee and lower back (did this while standing) • Check pulses • Check leg neurology
<p style="text-align: center;"><u>Knee Exam</u></p> <ul style="list-style-type: none"> • While standing: <ul style="list-style-type: none"> • Observe: <ul style="list-style-type: none"> • Varus/valgus or fixed flexion deformity • Scars, symmetry, swelling • Popliteal fossa: Baker's cyst • Gait • Squat down and duck walk • Observe on the bed: <ul style="list-style-type: none"> • Swelling, muscle wasting, scars, deformity • Actively push knee into bed (muscle bulk, fixed flexion deformity) • Straight leg raise: tests extensor mechanism • Palpate: <ul style="list-style-type: none"> • Warmth each side • Effusion: stroke test, patellar tap • Joint line (meniscal tears), collateral ligaments, ischial tuberosity and patellar ligament. Baker's cyst, popliteal pulse • Move: Flex both knees • Ligaments: (sit on foot, compare sides) <ul style="list-style-type: none"> • PCL: posterior sag and posterior draw test • ACL: anterior draw test, Lachman's, Pivot-shift • Collaterals: Varus and valgus stress test • McMurray's for meniscal tears • Patellar-femoral joint: Solomon's test. Feet over side: pointing straight ahead, raise leg (crepitus?), apprehension test • Hip, distal pulses and neurology 	<p style="text-align: center;"><u>Shoulder Exam</u></p> <ul style="list-style-type: none"> • Look (comparing both sides): <ul style="list-style-type: none"> • Skin: redness, scars • Shape (in front and behind): asymmetry, wasting, dislocation, swelling, sub-acromial sulcus • Feel: <ul style="list-style-type: none"> • Temperature • Around bones from clavicle to scapular • Tendons under acromion • In axilla: tenderness, lymph nodes • Move: <ul style="list-style-type: none"> • Abduction to 180° and adduction across chest • Flexion and extension • External rotation (forearms at 90°) • Internal rotation (scratch up back) • Rotator Cuff: <ul style="list-style-type: none"> • Supraspinatus: abduction from 0 - 30° against resistance with thumbs to the ground • Infraspinatus: externally rotate against resistance • Subscapularis: Lift-off test (try and push it away) • Stability: <ul style="list-style-type: none"> • Sulcus test: pull arm down and look for sulcus • Anterior draw test • Apprehension test • Push-ups against the wall • Examine neck and elbow • Distal pulses and neurology

<p><u>Respiratory Exam (Chest Only)</u></p> <ul style="list-style-type: none"> Introduce yourself, wash hands, light, position patient Observe: <ul style="list-style-type: none"> General: Cyanosis, pallor, cachexia, distress, LOC Chest: <ul style="list-style-type: none"> Respiratory distress, dyspnoea, rhythm Listen for cough, wheeze, hoarseness, stridor Scars Shape: scoliosis, kyphosis, pigeon Movement: accessory muscles, indrawing, paradoxical breathing of abdomen, expansion COUNT RESPIRATORY RATE Palpate: <ul style="list-style-type: none"> Neck: <ul style="list-style-type: none"> Nodes – especially supraclavicular Trachea – central, inspiratory tug Chest expansion Push sternum to spine (broken ribs) Tactile fremitus: 99 (on front and back) Percussion: Stony dull, dull, or hyper-resonant Auscultate: <ul style="list-style-type: none"> Breath Sounds (front and back): <ul style="list-style-type: none"> Air entry each side Vesicular or bronchial Wheeze, crackles, rubs Forced expiration Vocal resonance Peak Flow 	<p><u>CVS Exam (Precordium Only)</u></p> <ul style="list-style-type: none"> Introduce yourself, wash hands, light, patient at 45° Observe: <ul style="list-style-type: none"> General: cyanosis, pallor, cachexia, distress, LOC, Marfan's, Down's etc, <i>oedema</i> Chest: Scars, deformity, pacemakers, pulsations (look from side as well) JVP Palpation: <ul style="list-style-type: none"> Apex beat (and count down ribs – 2nd IC space at sternal angle): sustained, hyperkinetic, etc Parasternal heaves (RV activity), Aortic and pulmonary thrills Auscultation (ALWAYS time from carotid pulse): <ul style="list-style-type: none"> Diaphragm and bell at mitral, tricuspid, pulmonary and aortic areas Axilla with diaphragm (mitral regurg if systolic) Carotid arteries (bruit, aortic murmur) • To refine murmurs: <ul style="list-style-type: none"> Left lateral position: Mitral stenosis (bell) Leaning forward, full expiration, parasternal with diaphragm: Aortic regurg, hypertrophic cardiomyopathy Tricuspid murmurs: check JVP and pulsatile liver • Pulmonary oedema: Percuss and auscultate posterior
<p><u>Abdomen Exam (Abdomen only)</u></p> <ul style="list-style-type: none"> Introduce yourself, wash hands, light, patient at 0° Inspection: <ul style="list-style-type: none"> General: jaundice, pallor, pigmentation, weight/wasting, gynaecomastia, spider naevi, body hair, bruising Abdomen: <ul style="list-style-type: none"> Scars Distension Veins Striae Hernias, visible masses Pulsations (aorta, liver) • Palpation (warm hands, watch face): <ul style="list-style-type: none"> Light palpation Deep palpation: test for rebound Percuss then palpate liver (span, firm, nodular, tender, pulsatile). Test for movement on inspiration Percuss then palpate spleen Ballot kidneys Percuss for shifting dullness of ascites Bladder Auscultate: <ul style="list-style-type: none"> Bowel sounds Renal bruit Testicular, PR and inguinal hernias (cough) 	<p><u>Neurology Limb Exam</u></p> <ul style="list-style-type: none"> Observe: <ul style="list-style-type: none"> General: alertness, speech Posture Wasting, fasciculations, abnormal movements (tics, tremour, chorea, athetosis) • Power: compare sides, 0 – 5 Tone: of all movements: hypo or hyper tonic (rigidity, spasticity), ankle clonus Reflexes: <ul style="list-style-type: none"> Arm: triceps, biceps, supinator Leg: patellar, ankle, Plantar Sensory: <ul style="list-style-type: none"> Light touch Position sense Vibration Pinprick Temperature (same pathway as pinprick) • Coordination: <ul style="list-style-type: none"> Arms: rapid-alternating movements, finger-nose test, drift, flap Legs: heel-shin test, Romberg, heel-toe walking • Function: <ul style="list-style-type: none"> Legs: Gait, walk on heels (L5), toes (S1), crouch

<p><u>Examination of Cranial Nerves</u></p> <ul style="list-style-type: none"> • 2: Ophthalmic nerve: acuity, visual fields, fundoscopy • 3, 4 and 6: Oculomotor, Trochlear, and Abducens: <ul style="list-style-type: none"> • Pupils: ptosis, corneal light reflex, swinging light test (turn off light), accommodation reflex, squint • Eye movement: draw H, watch for lag or nystagmus, ask about diplopia • 5: Trigeminal: <ul style="list-style-type: none"> • Light touch and pin prick in all 3 divisions • Corneal reflex • Motor: <ul style="list-style-type: none"> • Wasting of muscles of mastication • Jaw opens in the midline • Clench jaw, palpate masseters • 7: Facial: <ul style="list-style-type: none"> • Wrinkle forehead • Show your teeth • Puff up cheeks • 8: Vestibulochoclear: <ul style="list-style-type: none"> • Rinne: conductive deafness if mastoid louder • Weber: hear loudest in good ear if sensori-neural deafness • 9 & 10: glossopharyngeal and Vagus: <ul style="list-style-type: none"> • Uvula in midline (say ‘ah’) • Swallowing and speech (ask about hoarseness) • 11: Accessory: Shrug shoulders, turn head against resistance • 12: Hypoglossal: wasting, fasciculation, protrudes in midline, ‘la la la’ quickly, push against inside of cheek 	<p><u>Examination of Leg Vasculature</u></p> <ul style="list-style-type: none"> • Inspection: <ul style="list-style-type: none"> • Colour • Presence of hairs • Varicose veins (while standing) • Dilated superficial veins (\Rightarrow DVT) • Ulcers • Swelling • Wasting – compare muscle bulk on each side • Clubbing of the toes • Oedema • Palpation: <ul style="list-style-type: none"> • Compare size, tenderness and warmth of calves • Oedema • Temperature of feet • Capillary return • Sensation • Veins: hard \Rightarrow thromboses. Tender \Rightarrow thrombophlebitis • Peripheral pulses: <ul style="list-style-type: none"> • Femoral: Palpate and auscultate for bruits • Palpate popliteal, posterior tibial, dorsalis pedis • Buerger’s test: <ul style="list-style-type: none"> • Elevate leg to 45°. Pallor is rapid if poor arterial supply • Then hand over bed. Cyanosis rapid if poor arterial supply • Bed side test: ABI (Ankle Brachial Index): ultrasound comparison of blood flow in the arm and leg
<p><u>Abnormal Menstruation</u></p> <ul style="list-style-type: none"> • Basic Menstrual History: <ul style="list-style-type: none"> • LMP • Normal cycle length, days of bleeding, regularity • How heavy is bleeding (number of pads, clots, etc) • Associated pain • Other bleeding: between periods, post-coital • Age at menarche • Age at menopause, post menopausal symptoms and any bleeding • Contraception • Amenorrhoea: <ul style="list-style-type: none"> • Primary: Never menstruated. Rare. Turner’s, Testicular feminisation, etc • Secondary: <ul style="list-style-type: none"> • Pregnancy related: pregnant or breast feeding • PoP, Depot • Stress: Anorexia, athlete, disease (\downarrowweight) • Prolactinoma \rightarrow \downarrowpituitary function, visual fields, headaches • Ovarian causes (PCO, tumours): virilisation, \uparrowweight • Premature menopause • Hyperthyroidism • Menorrhagia: <ul style="list-style-type: none"> • Young: abnormal menstrual bleeding • Older: IUD, fibroids, endometriosis, polyps, cancer • Infection (any pain, fevers, discharge) • Hypothyroidism \rightarrow cold intolerance, weight gain 	<p><u>Gynaecological History</u></p> <ul style="list-style-type: none"> • Introductory data: <ul style="list-style-type: none"> • Age • Gravidity (pregnancies) + Parity (Deliveries) • LMP • HPC: including details of bleeding, pain, discharge and urinary symptoms • Past Gynae History: <ul style="list-style-type: none"> • Age at menarche • Menstrual history • Past gynae problems/procedures/abdo surgery • Sexual history • Current/past contraception • Past STDs • Incontinence • Smear history • Past Obstetric history • PMH • Medications • FHx: mother or sisters with gynae/obstetric problems • Social Hx: Relationship status, sexual activity, alcohol & smoking, occupation, any inter-personal violence or abuse

<p><u>Obstetric History</u></p> <ul style="list-style-type: none"> Introductory data: <ul style="list-style-type: none"> Age Gravidity (pregnancies) + Parity (Deliveries) LMP Current pregnancy: <ul style="list-style-type: none"> Due date (check accuracy) Contractions/pain Bleeding Discharge Fetal movements Past Obstetric History: <ul style="list-style-type: none"> When was it Antenatal problems (eg ↑BP, diabetes, etc) Delivered: pre-term, post-term? Delivery: vaginal, C-section Weight of baby Post partum: any bleeding, infection, depression Baby: any problems – how are they now Feeding: breast or bottle Past Gynae history: <ul style="list-style-type: none"> Previous problems: infection, surgery, etc Contraceptive history Smear history PMH: hypertension, DM, heart disease, asthma, DVTs, infections (esp STIs, Hep B, Tb), depression, endocrine Medication: especially folate FHx: DVTs, birth defects, multiple births, pregnancy problems Social: relationship, smoking & alcohol, occupation 	<p><u>Pelvic Pain</u></p> <ul style="list-style-type: none"> Pain with sex = dyspareunia <ul style="list-style-type: none"> Superficial: eg HSV, atrophy, vaginismus Deep: pelvic disease (eg endometriosis, PID), post-hysterectomy Period pain = dysmenorrhoea: <ul style="list-style-type: none"> Primary: Young, first 2 days of menses, no organ pathology, started at menarche and not getting worse Secondary: Older, prior to and through out bleeding, pelvic disease/infection, PMS For > 6 months = Chronic pelvic pain <ul style="list-style-type: none"> Intermittent (with sex/menses, etc) or continuous Gynae: dysmenorrhoea, endometriosis, adenomyosis, PID, prolapse, post-delivery trauma, etc Non-gynae: UTI, IBS, diverticular, musculo-skeletal <p><u>Sexual History</u></p> <ul style="list-style-type: none"> Number & duration of relationships Previous similar symptoms UTI questions: frequency, discharge, abdo pain, testicular pain, joint pain Screen for high risk behaviour: <ul style="list-style-type: none"> Alcohol and drug use Unprotected sex Multiple partners Anal/oral sex
<p><u>Psych History</u></p> <ul style="list-style-type: none"> Identifying data: name, age, occupation HPC (including when did you last feel well, what's your worst worry) Systematic enquiry: <ul style="list-style-type: none"> Anxiety + phobias Mood Psychotic Suicidality Cognitive Neurophysiological: sleep, appetite, weight Alcohol and drug Impulse-control screen Medications Past psych history PMH Family: anyone had psych illness, had a breakdown, attempted suicide, had an A&D problem Social: including personal history, past difficulties (abuse, legal, relationships, etc) Mental state: appearance and behaviour, speech, mood, affect, thought form, thought content, suicidal ideation, perceptual phenomena, cognition, intelligence, insight and judgement, rapport 	<p><u>Suicide Assessment</u></p> <ul style="list-style-type: none"> History: <ul style="list-style-type: none"> Ideation: <ul style="list-style-type: none"> Do you think a lot about death Do you want to die – or want others to know how bad it is Do you have the means What's stopped you so far How do you feel about accepting help Past attempts: <ul style="list-style-type: none"> What did you do Why did you do it What was the final straw Did you leave a note What stop you going through with it Risk assessment: <ul style="list-style-type: none"> Predisposing factors: Family history, psych illness, alcohol and drug problem, suicide exposure, other illness, age and sex, living alone Precipitating factors: Stressful events, current mood, thoughts about the future, mental state, current plans, availability of method Protective factors: cognitive flexibility, social supports, hopefulness, treatment of disorders, responsibility for children

<u>Shortness of Breath</u>	<u>Key Differentials</u>
<ul style="list-style-type: none"> Very sudden: <ul style="list-style-type: none"> MI: palpitations, pain, anxious, risk factors (hypertension, diabetes, ↑lipids, smoking, previous MI, stroke or claudication, FHx) PE: Palpitations, Leg swelling, immobility, surgery, pregnancy, past or family history Pneumothorax Over a few hours: <ul style="list-style-type: none"> Asthma: night cough, wheeze, previous history. <i>Test peak flow</i> Pneumonia: fevers, sweats, cough, sputum, blood, pain with coughing Gradual: <ul style="list-style-type: none"> Heart failure: oedema, tired, orthopnoea, PND, history or risk factors for IHD Anaemia Carcinoma Others: <ul style="list-style-type: none"> Metabolic acidosis (eg Diabetic ketoacidosis) Psychiatric – eg anxiety Remember to ask about medications and smoking Investigations: <ul style="list-style-type: none"> Examine the patient, including BP, pulse & JVP Peak flow Bloods: FBC, Electrolytes, cardiac enzymes ABGs Sputum/blood cultures CXR, ECG Treatment: include O₂ 	<ul style="list-style-type: none"> Sleepiness/Fatigue: <ul style="list-style-type: none"> Sleep disturbance/restriction (?anxiety) Sleep apnoea Depression Hypothyroidism Heart failure Anaemia Acute or chronic disease (eg EBV) Drugs: β-blockers, anti-histamines, sedatives, alcohol Passing out: <ul style="list-style-type: none"> Arrhythmia Epilepsy (any aura, witness report, post-ictal state, past head injury) CVA Postural hypotension Vasovagal faint Hypoglycaemia Fall
<u>ECG Interpretation</u> <ul style="list-style-type: none"> Rate (brady or tachycardia). 300/no of big squares Rhythm: Relationship of P waves to QRS → sinus arrhythmia, supraventricular arrhythmia, escape beats Cardiac Axis: Normal if I and II positive <ul style="list-style-type: none"> Left deviation = I+, II and III – Right deviation = I-, II +/-, III + Description of P wave: <ul style="list-style-type: none"> Peaked P: RA hypertrophy Twin peaked P: LA hypertrophy Large P → ↓K, small P → ↑K Conduction intervals: Start of P to start of QRS = 3 – 5 small squares (0.12 – 0.2 secs) Description of QRS: <ul style="list-style-type: none"> Normal <= 3 small squares. > BBB or ventricular Q waves (or 25% of QRS). Anterior: V2, V3. Lateral: I, II, VL, V3-6. Inferior: III and VF Bundle Branch: Marrow and William in V1/V6 RV Hypertrophy: R in V1/2 + S in V5/6 LV Hypertrophy: S in V1/2 + R in V5/6 ST Segment: <ul style="list-style-type: none"> Raised: infarction. Anterior V5, V6. Inferior III, VF Depressed: ischaemia T wave: Normally inverted in VR and V1. Abnormal if –ive in I, II, V4-6. If not full thickness infarct → T wave inversion but no Q wave. Digoxin: T wave inversion, sloping ↓ of ST. ↓K → flat, ↑K → wide, peaked QT interval 	<u>Paediatric Differentials</u> <ul style="list-style-type: none"> Quick screen for severity of illness: responsiveness, feeding, urine, colour, breathing Fever in a child without clear focus: <ul style="list-style-type: none"> Infection: UTI, bacteraemia, meningitis Rheumatic Fever Poisoning Leukaemia Drug Fever Gastroenteritis in a child: <ul style="list-style-type: none"> Infection: Rotavirus, campylobacter, protozoa Systemic: UTI, Pneumonia, otitis media Surgical: appendicitis, intussusception, obstruction (eg hernia), pyloric stenosis, torsion, secondary to adhesions Other: diabetic ketoacidosis, antibiotic diarrhoea, poisoning PR Bleeding: necrotising enterocolitis, intussusception, IBD (unlikely), familial polyps Abdo pain is likely to be benign if: didn't know about it till the child said, they're distractible from it, it is central, no sleep disturbance, no symptoms, intermittent Coma: hypoxic, epileptic, trauma, infection, poison, renal failure, hypo/hyperglycaemia, hyper/hypo-thermia, hypertension

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